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=> d his

     (FILE 'REGISTRY' ENTERED AT 12:06:23 ON 20 SEP 2004)
                DEL HIS Y
                E NATEGLINIDE/CN
L1             1 S E3
L2               STR 105816-04-4
L3            35 S L2 FUL FAM
                 SAVE L3 TEMP HECTOR/A

     FILE 'CAPLUS' ENTERED AT 12:07:34 ON 20 SEP 2004
L4           302 S L3
L5        110399 S POLYMORPH?
L6       1165131 S CRYS?
L7            11 S L4 AND L5
L8            24 S L4 AND L6
L9            24 S L7 OR L8

     FILE 'BIOSIS, MEDLINE' ENTERED AT 12:10:15 ON 20 SEP 2004
L10          351 S L3
L11       233880 S CRYS?
L12            4 S L10 AND L11

     FILE 'USPATFULL' ENTERED AT 12:11:39 ON 20 SEP 2004
L13           90 S L3
L14           12 S L13 AND (CRYS?)/TI,AB,CLM

     FILE 'CAPLUS, BIOSIS, MEDLINE, USPATFULL' ENTERED AT 12:12:23 ON 20 SEP
     2004
L15           35 DUP REM L9 L12 L14 (5 DUPLICATES REMOVED)
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=> fil caplus biosis medline uspatfull
FILE 'CAPLUS' ENTERED AT 12:12:51 ON 20 SEP 2004
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FILE 'MEDLINE' ENTERED AT 12:12:51 ON 20 SEP 2004

FILE 'USPATFULL' ENTERED AT 12:12:51 ON 20 SEP 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> d que l15
L2                STR
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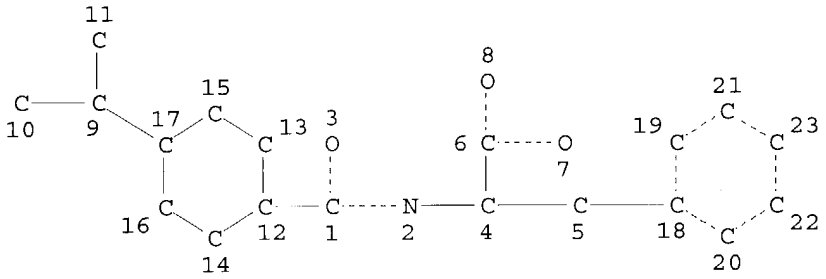


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  23

STEREO ATTRIBUTES: NONE
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L4           302 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3
L5        110399 SEA FILE=CAPLUS ABB=ON  PLU=ON  POLYMORPH?/OBI
L6       1165131 SEA FILE=CAPLUS ABB=ON  PLU=ON  CRYS?/OBI
L7            11 SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND L5
L8            24 SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND L6
L9            24 SEA FILE=CAPLUS ABB=ON  PLU=ON  L7 OR L8
L10          351 SEA L3
L11       233880 SEA CRYS?
L12            4 SEA L10 AND L11
L13           90 SEA FILE=USPATFULL ABB=ON  PLU=ON  L3
L14           12 SEA FILE=USPATFULL ABB=ON  PLU=ON  L13 AND (CRYS?)/TI,AB,CLM
L15           35 DUP REM L9 L12 L14 (5 DUPLICATES REMOVED)


=> d bib ab hitstr l15 1-35

L15  ANSWER 1 OF 35  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:648496  CAPLUS
DN   141:179640
TI   Preparation of a polymorphic crystalline form of the
     antidiabetic agent nateglinide
```

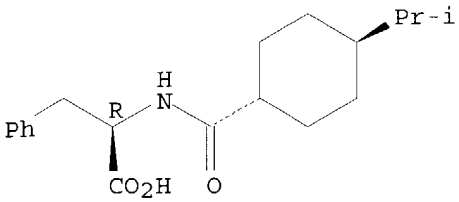
NPA

IN Frenkel, Gustavo; Gome, Boaz; Wizel, Shlomit
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SO PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004067496	A1	20040812	WO 2004-US839	20040113
	W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
	WO 2004009532	A1	20040129	WO 2003-US322375	20030718
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004181089	A1	20040916	US 2003-622905	20030718
PRAI	US 2003-442109P	P	20030123		
	US 2003-449791P	P	20030224		
	US 2003-479016P	P	20030616		
	US 2003-622905	A2	20030718		
	WO 2003-US22375	A2	20030718		
	US 2003-693166	A2	20031023		
	US 2003-746697	A2	20031224		
	US 2002-396904P	P	20020718		
	US 2002-413622P	P	20020925		
	US 2002-414199P	P	20020926		
	US 2002-423750P	P	20021105		
	US 2002-432093P	P	20021210		
	US 2002-432962P	P	20021212		
	US 2003-614266	A	20030703		

AB The preparation of a polymorphic crystalline form (e.g., form U) of the antidiabetic agent nateglinide is described.
IT **105816-04-4**, Nateglinide
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of a **polymorphic crystalline** form of the antidiabetic agent nateglinide)
RN 105816-04-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



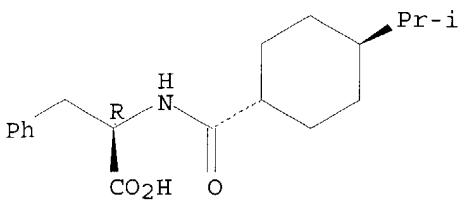
L15 ANSWER 2 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:203799 CAPLUS
DN 140:241062
TI Process for the formation of a **crystalline polymorphic** form of nateglinide
IN Reguri, Buchi Reddy; Kadaboina, Rajasekhar; Polavarapu, Srinivas
PA Reddy's Laboratories Limited, India; Reddy's Laboratories, Inc.
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004020396	A1	20040311	WO 2003-US26880	20030827
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004077725	A1	20040422	US 2003-649380	20030827
PRAI	IN 2002-MA631	A	20020828		

N/A

AB A crystalline polymorphic form of nateglinide are described and its X-ray diffraction pattern presented.
IT **105816-04-4P**, Nateglinide
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(process for the formation of a **crystalline polymorphic** form of nateglinide)
RN 105816-04-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:80637 CAPLUS
DN 140:151932
TI Preparation of **polymorphic** forms of nateglinide
IN Yahalomi, Ronit; Shapior, Evgeny; Dolitzky, Ben-zion; Gozlan, Yigael; Gome, Boaz
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceutical Usa, Inc.
SO PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004009532	A1	20040129	WO 2003-US22375	20030718
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004152782	A1	20040805	US 2003-614266	20030703
	US 2004116526	A1	20040617	US 2003-623237	20030718
	WO 2004067496	A1	20040812	WO 2004-US839	20040113
	W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
PRAI	US 2002-396904P	P	20020718		
	US 2002-413622P	P	20020925		
	US 2002-414199P	P	20020926		
	US 2002-423750P	P	20021105		
	US 2002-432093P	P	20021210		
	US 2002-432962P	P	20021212		
	US 2003-442109P	P	20030123		
	US 2003-449791P	P	20030224		
	US 2003-479016P	P	20030616		
	US 2003-614266	A	20030703		
	US 2002-393495P	P	20020703		

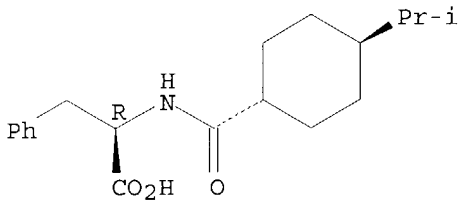
US 2003-622905 A2 20030718
WO 2003-US22375 A2 20030718
US 2003-693166 A2 20031023
US 2003-746697 A2 20031224

AB The invention discloses the preparation of 26 characterized forms of nateglinide (forms A, C, D, F, G, I, J, K, L, M, N, O, P, Q, T, U, V, Y, α, β, γ, δ, ε, σ, θ and Ω). Most of the forms are solvates (with the exception of forms L, P, U, α, δ and σ). Polymorphic forms are characterized by their mp, DSC, XRPD, FTIR; form interconversion is also discussed. For example, D-phenylalanine is reacted with trans-[[4-(isopropyl)cyclohexanee]carbonyl]chloride (i. NaOHaq; ii. H2SO4). The wet cake of nateglinide is dissolved in EtOAc, the aqueous phase is removed and the resulting solution heated to 50° under reduced pressure and added to hot heptane. The resulting solution is cooled and seeded with the B-form to afford the δ-form (33% yield).

IT **105816-04-4P**, Nateglinide
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(preparation of **polymorphic** forms of nateglinide)

RN 105816-04-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

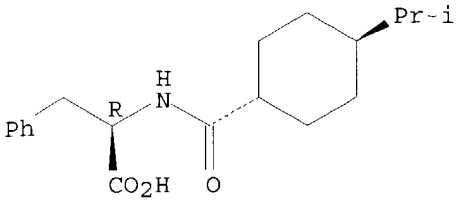
Absolute stereochemistry. Rotation (-).



IT **105816-04-4DP**, Nateglinide, **polymorphs**
651353-42-3P 651353-43-4P 651353-44-5P
651353-45-6P 651353-46-7P 651353-47-8P
651353-48-9P 651353-49-0P 651353-50-3P
651353-51-4P 651353-52-5P 651353-53-6P
651353-54-7P
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of **polymorphic** forms of nateglinide)

RN 105816-04-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

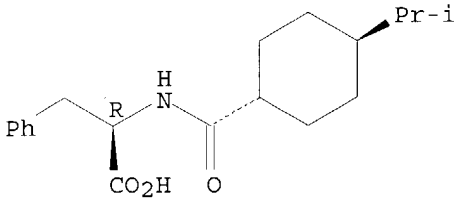


RN 651353-42-3 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with methanol (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry. Rotation (-).



CM 2

CRN 67-56-1
CMF C H4 O

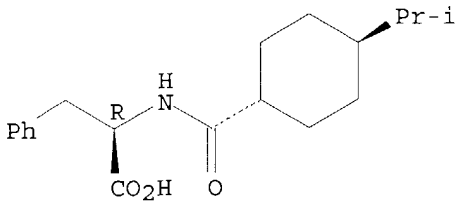
H_3C-OH

RN 651353-43-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with ethanol (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry. Rotation (-).



CM 2

CRN 64-17-5
CMF C2 H6 O

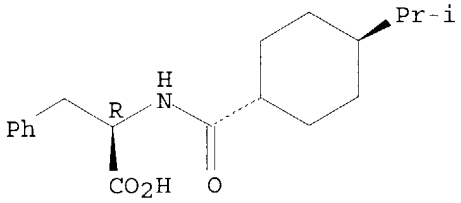
H_3C-CH_2-OH

RN 651353-44-5 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1-butanol (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry. Rotation (-).



CM 2

CRN 71-36-3
CMF C4 H10 O

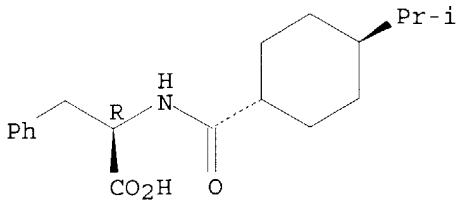
$H_3C-CH_2-CH_2-CH_2-OH$

RN 651353-45-6 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1-propanol (9CI) (CA INDEX NAME)

CM 1

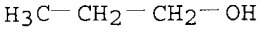
CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry. Rotation (-).



CM 2

CRN 71-23-8
CMF C3 H8 O

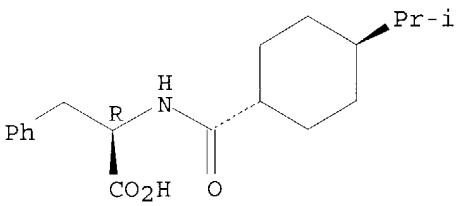


RN 651353-46-7 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with N,N-dimethylacetamide (9CI) (CA INDEX NAME)

CM 1

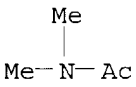
CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry. Rotation (-).



CM 2

CRN 127-19-5
CMF C4 H9 N O

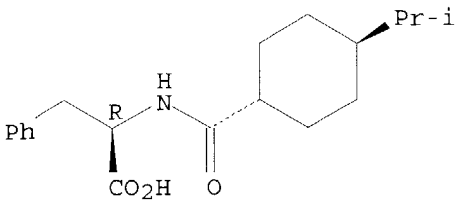


RN 651353-47-8 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1-methyl-2-pyrrolidinone (9CI) (CA INDEX NAME)

CM 1

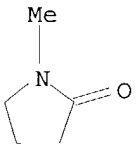
CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry. Rotation (-).



CM 2

CRN 872-50-4
CMF C5 H9 N O



RN 651353-48-9 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with N,N-dimethylformamide (9CI) (CA INDEX NAME)

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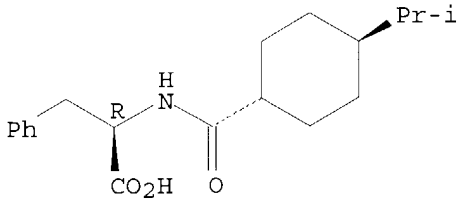
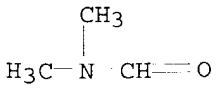
CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry. Rotation (-).



CM 2

CRN 68-12-2
CMF C3 H7 N O

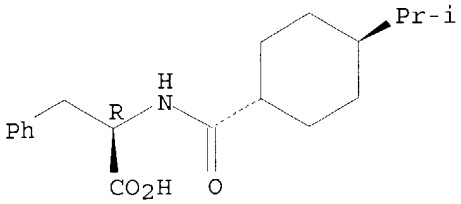


RN 651353-49-0 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1,2-dimethoxyethane (9CI) (CA INDEX NAME)

CM 1

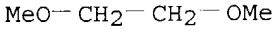
CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry. Rotation (-).



CM 2

CRN 110-71-4
CMF C4 H10 O2

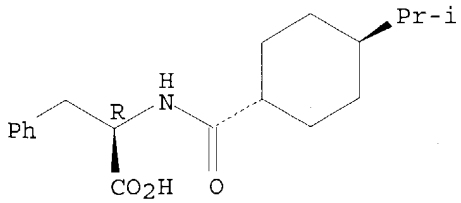


RN 651353-50-3 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with dimethylbenzene (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry. Rotation (-).



CM 2

CRN 1330-20-7
CMF C8 H10
CCI IDS

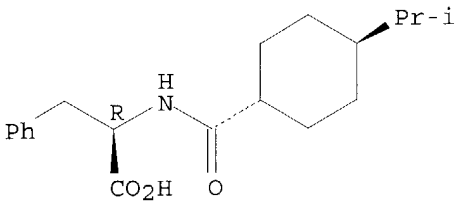
2 (D1—Me)

RN 651353-51-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with tetrachloromethane (9CI) (CA INDEX NAME)

CM 1

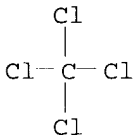
CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry. Rotation (-).



CM 2

CRN 56-23-5
CMF C Cl4

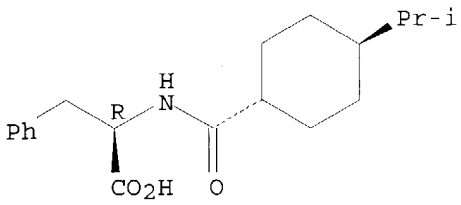


RN 651353-52-5 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1,2-dichloroethane (9CI) (CA INDEX NAME)

CM 1

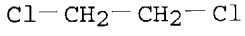
CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry. Rotation (-).



CM 2

CRN 107-06-2
CMF C2 H4 Cl2

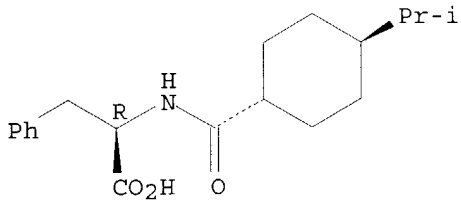


RN 651353-53-6 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with trichloromethane (9CI) (CA INDEX NAME)

CM 1

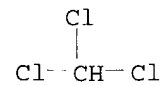
CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry. Rotation (-).



CM 2

CRN 67-66-3
CMF C H Cl3

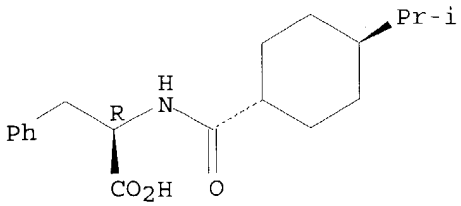


RN 651353-54-7 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with heptane (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry. Rotation (-).



CM 2

CRN 142-82-5
CMF C7 H16

Me— $(CH_2)_5$ —Me

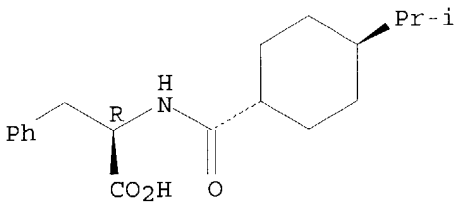
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 35 USPATFULL on STN
AN 2004:197476 USPATFULL
TI Process for preparing nateglinide and intermediates thereof
IN Yahalomi, Ronit, Kiryat Bialik, ISRAEL
Shapiro, Evgeny, Haifa, ISRAEL
Dolitzky, Ben-Zion, Petach Tiqva, ISRAEL
Gozlan, Yigael, Ramot Sapir, ISRAEL
PI US 2004152782 A1 20040805
AI US 2003-614266 A1 20030703 (10)
PRAI US 2002-393495P 20020703 (60)
US 2002-396904P 20020718 (60)
US 2002-413622P 20020925 (60)
US 2002-414199P 20020926 (60)
US 2002-423750P 20021105 (60)
US 2002-432093P 20021210 (60)
US 2002-432962P 20021212 (60)
US 2003-442109P 20030123 (60)
US 2003-449791P 20030224 (60)
DT Utility
FS APPLICATION
LREP KENYON & KENYON, ONE BROADWAY, NEW YORK, NY, 10004
CLMN Number of Claims: 57
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 906
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Provided is a process for preparation of an intermediate in the synthesis of nateglinide. Trans-4-isopropylcyclohexane acid chloride is formed by reacting 4-isopropylcyclohexanecarboxyl acid with thionyl chloride in the presence of an effective amount of an organic amide.

Also provided are processes for preparation of nateglinide by acylation of a suitable salt of D-phenylalanine with trans-4-isopropylcyclohexane acid chloride in both a single and a two phase system, and in water free of a co-solvent.

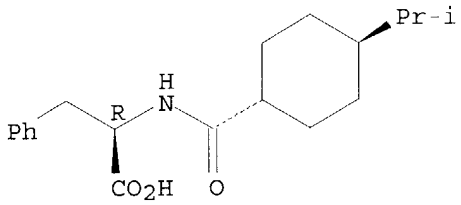
IT **105816-04-4P**, Nateglinide
(process for preparation of nateglinide)
RN 105816-04-4 USPATFULL
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI)
(CA INDEX NAME)

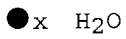
Absolute stereochemistry. Rotation (-).



IT **173653-89-9**
(properties of nateglinide hydrate)
RN 173653-89-9 USPATFULL
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, hydrate
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



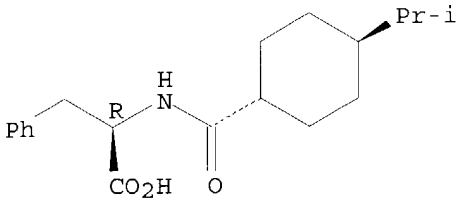


L15 ANSWER 5 OF 35 USPATFULL on STN
AN 2004:185129 USPATFULL
TI Combination of organic compounds
IN Villhauer, Edwin Bernard, Morristown, NJ, UNITED STATES
PI US 2004143015 A1 20040722
AI US 2003-471253 A1 20030910 (10)
WO 2002-EP2665 20020311
DT Utility
FS APPLICATION
LREP NOVARTIS, CORPORATE INTELLECTUAL PROPERTY, ONE HEALTH PLAZA 430/2, EAST HANOVER, NJ, 07936-1080
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1075
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a combination of organic compounds which comprises at least two antidiabetic agents, preferably with different modes of action, in which the active ingredients are in each case present in free form or in the form of a pharmaceutically

acceptable salt and, optionally, at least on pharmaceutically acceptable carrier, for simultaneous, separate or sequential use.

IT **105816-04-4**, Nateglinide
(pharmaceutical compns. containing combination of antidiabetic compds.)
RN 105816-04-4 USPATFULL
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

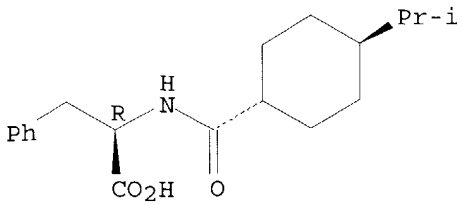
Absolute stereochemistry. Rotation (-).



L15 ANSWER 6 OF 35 USPATFULL on STN
AN 2004:152304 USPATFULL
TI Polymorphic forms of nateglinide
IN Yahalomi, Ronit, Kiryat Bialik, ISRAEL
Shapiro, Evgeny, Haifa, ISRAEL
Dolitzky, Ben-Zion, Petach Tiqva, ISRAEL
Gozlan, Yigael, Ramot Sapir, ISRAEL
Gome, Boaz, Rishon-Lezion, ISRAEL
PI US 2004116526 A1 20040617
AI US 2003-623237 A1 20030718 (10)
PRAI US 2002-396904P 20020718 (60)
US 2002-413622P 20020925 (60)
US 2002-414199P 20020926 (60)
US 2002-423750P 20021105 (60)
US 2002-432093P 20021210 (60)
US 2002-432962P 20021212 (60)
US 2003-442109P 20030123 (60)
US 2003-449791P 20030224 (60)
US 2003-479016P 20030616 (60)
DT Utility
FS APPLICATION
LREP KENYON & KENYON, ONE BROADWAY, NEW YORK, NY, 10004
CLMN Number of Claims: 55
ECL Exemplary Claim: 1
DRWN 64 Drawing Page(s)
LN.CNT 1830
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Provides are **crystalline** forms of nateglinide, labeled Forms A, C, D, F, G, I, J, K, L, M, N, O, P, Q, T, U, V, Y, α, β, γ, δ, ε, σ, 0 and Ω, processes for their preparation and processes for preparation of other **crystalline** forms of nateglinide. Also provided are their pharmaceutical formulations and methods of administration.

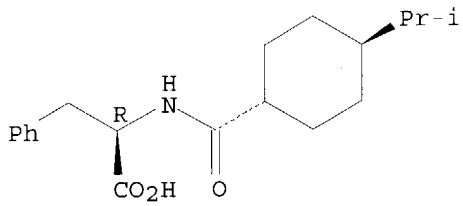
IT **105816-04-4P**, Nateglinide
(process for preparation of nateglinide)
RN 105816-04-4 USPATFULL
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **173653-89-9**
(properties of nateglinide hydrate)
RN 173653-89-9 USPATFULL
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, hydrate (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

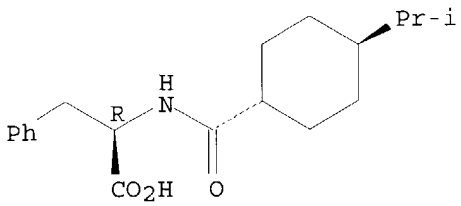


●x H_2O

L15 ANSWER 7 OF 35 USPATFULL on STN
AN 2004:101855 USPATFULL
TI **Crystalline** form of N-(trans-4-isopropylcyclohexane carbonyl)-D-phenylalanine and process for preparation thereof
IN Reguri, Buchi Reddy, Hyderabad, INDIA
Kadaboina, Rajasekhar, Hyderabad, INDIA
Polavarapu, Srinivas, Hyderabad, INDIA
PA DR. REDDY'S LABORATORIES LIMITED (non-U.S. corporation)
DR. REDDY'S LABORATORIES, INC. (non-U.S. corporation)
PI US 2004077725 A1 20040422
AI US 2003-649380 A1 20030827 (10)
PRAI IN 2002-6312002 20020828
DT Utility
FS APPLICATION
LREP Janet I. Cord, Ladas & Parry, 26 West 61 Street, New York, NY, 10023
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 2 Drawing Page(s)
LN.CNT 863
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A new **crystalline** form of nateglinide is provided. The new **crystalline** form is described by X-ray powder diffraction. Processes for making the new **crystalline** form of nateglinide are also provided.
IT **105816-04-4P**, Nateglinide
(process for the formation of a crystalline polymorphic form of nateglinide)
RN 105816-04-4 USPATFULL

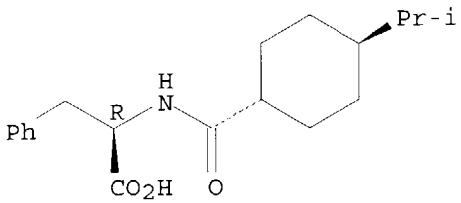
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



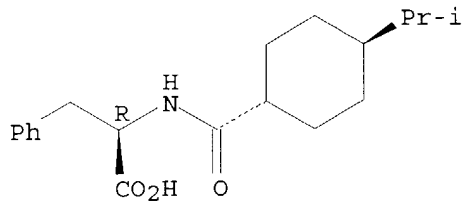
L15 ANSWER 8 OF 35 USPATFULL on STN
AN 2004:39640 USPATFULL
TI Methods for producing nateglinide **crystals**
IN Takahashi, Daisuke, Yokkaichi-Shi, JAPAN
Nishi, Seiichi, Yokkaichi-Shi, JAPAN
Takahashi, Satoji, Yokkaichi-Shi, JAPAN
PA AJINOMOTO CO. INC., Tokyo, JAPAN (non-U.S. corporation)
PI US 2004030182 A1 20040212
AI US 2003-418105 A1 20030418 (10)
RLI Continuation of Ser. No. WO 2001-JP9069, filed on 16 Oct 2001, UNKNOWN
PRAI JP 2000-317604 20001018
DT Utility
FS APPLICATION
LREP OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C., 1940 DUKE STREET, ALEXANDRIA, VA, 22314
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 387
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB There is provided methods for producing nateglinide **crystals**, which comprises the steps of adding an acid(s) to a reaction mixture containing nateglinide to make it acidic, the reaction mixture being obtained by reacting trans-4-isopropylcyclohexylcarbonyl chloride with D-phenylalanine in a mixed solvent of ketone solvent and water in the presence of an alkali; and then adjusting the temperature of the mixture to 58° C. to 72° C. and the concentration of ketone solvent to more than 8 wt % and less than 22 wt % to conduct precipitation of nateglinide **crystals.** This producing method is the industrially beneficial methods for **crystallization** of nateglinide.
IT **105816-04-4P**, Nateglinide
(process for producing nateglinide crystals)
RN 105816-04-4 USPATFULL
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 9 OF 35 USPATFULL on STN
AN 2004:39426 USPATFULL
TI Nateglinide-containing hydrophilic pharmaceutical preparation
IN Ninomiya, Nobutaka, Kawasaki-Shi, JAPAN
Makino, Chisato, Kawasaki-Shi, JAPAN
Yabuki, Akira, Kawasaki-Shi, JAPAN
PA AJINOMOTO CO. INC, Tokyo, JAPAN (non-U.S. corporation)
PI US 2004029968 A1 20040212
AI US 2003-420886 A1 20030423 (10)
RLI Continuation of Ser. No. WO 2001-JP9292, filed on 23 Oct 2001, UNKNOWN
PRAI JP 2000-324374 20001024
DT Utility
FS APPLICATION
LREP OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C., 1940 DUKE STREET, ALEXANDRIA, VA, 22314
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN 8 Drawing Page(s)
LN.CNT 486
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB There is provided a nateglinide-containing hydrophilic pharmaceutical preparation comprising nateglinide B-type **crystals** as an effective ingredient, the contact angle of the surface of said preparation to water becoming 111 degree or less by incorporating in said preparation at least one hydrophilic substance selected from the groups consisting of hydrophilic polymers, surfactants, sugars, sugar alcohols and salts. This preparation is one having sufficient immediate-release and high dissolution properties, and can be easily prepared.
IT **105816-04-4**, Nateglinide
(hypoglycemic hydrophilic drug prepns. containing)
RN 105816-04-4 USPATFULL
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

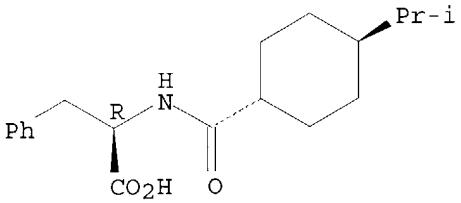
Absolute stereochemistry. Rotation (-).



L15 ANSWER 10 OF 35 USPATFULL on STN
AN 2004:19511 USPATFULL

TI Nateglinide-containing preparation
IN Ninomiya, Nobutaka, Kawasaki-Shi, JAPAN
Makino, Chisato, Kawasaki-Shi, JAPAN
Yabuki, Akira, Kawasaki-Shi, JAPAN
PA AJINOMOTO CO. INC., Tokyo, JAPAN (non-U.S. corporation)
PI US 2004014815 A1 20040122
AI US 2003-421898 A1 20030424 (10)
RLI Continuation of Ser. No. WO 2001-JP9291, filed on 23 Oct 2001, UNKNOWN
PRAI JP 2000-324373 20001024
DT Utility
FS APPLICATION
LREP OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C., 1940 DUKE STREET, ALEXANDRIA, VA, 22314
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 9 Drawing Page(s)
LN.CNT 537
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention discloses, as a immediate-release preparation useful as an antidiabetic, a nateglinide-containing preparation comprising nateglinide as an active ingredient wherein the nateglinide is amorphous.
IT **105816-04-4**, Nateglinide
(antidiabetic solid prepns. containing amorphous nateglinide and hydrophilic carriers)
RN 105816-04-4 USPATFULL
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 11 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:892741 CAPLUS
DN 139:369757
TI Process for the preparation of a **crystal polymorphic** form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide)
IN Rajamahendra, Shanmughasamy; Aswathanarayanappa, Chandrashekar; Puthiaparampil, Tom Thomas; Sridharan, Madhavan; Ganesh, Sambasivam
PA Biocon India Limited, India
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003093222	A1	20031113	WO 2002-IN114	20020429

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,

HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI WO 2002-IN114 20020429

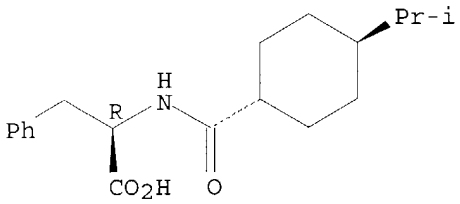
AB Novel polymorph Form C of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (I; i.e., nateglinide) is produced having a different IR spectrum and X-ray diffraction patterns (presented) from previously known forms of I.

IT **105816-04-4P**, Nateglinide
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); PREP (Preparation); PROC (Process)
(process for the preparation of a **crystal polymorphic** form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide))

RN 105816-04-4 CAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

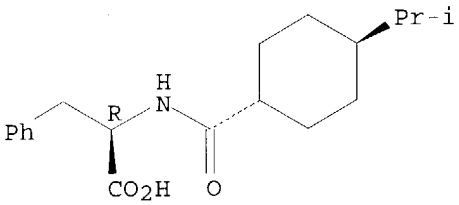
L15 ANSWER 12 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:837030 CAPLUS
DN 139:341723
TI Novel nateglinide **crystals**
IN Koguchi, Yoshihito; Nakao, Tomoko; Sumikawa, Michito
PA Ajinomoto Co., Inc., Japan
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003087039	A1	20031023	WO 2003-JP4686	20030414

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,

NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI JP 2002-111963 A 20020415
AB A type crystal (powder X-ray diffraction main peaks: 4.4°, 5.2°, 15.7°, 18.5° (2 theta)), M type crystal (powder X-ray diffraction main peaks: 6.0°, 14.2°, 15.2°, 18.8° (2 theta)), and P type crystal (powder X-ray diffraction main peaks: 4.8°, 5.3°, 14.3°, 15.2° (2 theta)) of nateglinide, which are all novel crystals, can be prepared by a method comprising dissolving nateglinide in a solvent exhibiting high solubility for nateglinide and then adding a solvent exhibiting poor solubility for nateglinide or dissolving nateglinide in a mixed solvent comprising a solvent exhibiting high solubility for nateglinide and a solvent exhibiting poor solubility for nateglinide and then cooling the resulting nateglinide solution to precipitate crystals, subjecting the product to filtration, and then drying at a specific temperature Nateglinide is a known antidiabetic.
IT **105816-04-4P**, Nateglinide
RL: PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of A, M, and P type nateglinide **crystals** by **crystallization** from mixture of solvents)
RN 105816-04-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

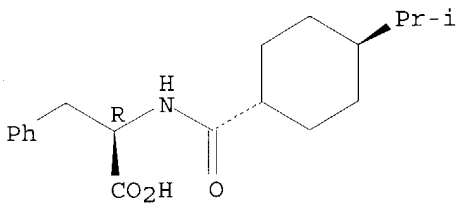
L15 ANSWER 13 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:837029 CAPLUS
DN 139:328379
TI **Crystal polymorphism** of nateglinide
IN Sutton, Paul Allen
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003087038	A1	20031023	WO 2003-EP3864	20030414

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR
PRAI US 2002-372625P P 20020415
AB New crystal forms of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (i.e., nateglinide) are produced by dissolving nateglinide in any of its forms, including solvates, in an organic solvent to form a solution followed by precipitation of nateglinide from the solution, and isolating and drying the precipitated crystal form of nateglinide. The precipitation of nateglinide may be induced either by cooling the solution, or by addition of another solvent which is miscible with the first solvent but in which nateglinide is only poorly soluble, or by combination of the two. Depending on the solvent a specific crystal form of nateglinide may be obtained, e.g., the R'-type crystal form of nateglinide produced by the described method has a different m.p., infra red spectra and X-ray diffraction patterns from the previously known crystal forms of nateglinide.
IT **105816-04-4**, Nateglinide
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); PROC (Process)
(**crystal polymorphism** of nateglinide)
RN 105816-04-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 14 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:221492 CAPLUS
DN 138:243310
TI Novel stable **crystal** form of N-trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine and process of preparation
IN Shah, Vrajesh; Hitkari, Anurag; Deo, Keshav; Rengaraju, Srinivasan
PA Alembic Limited, India
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003022251	A1	20030320	WO 2001-IB2080	20011105

W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, ES, GD, GE, HR, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PH, PL, RO, SG, SI, SK, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1435912 A1 20040714 EP 2001-978760 20011105

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI IN 2001-MU871 A 20010912

IN 2001-MU872 A 20010912

WO 2001-IB2080 W 20011105

AB A stable crystal form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (I) may be produced by crystallization of I with a solvent at 25 - 38 °C and forming crystals in the solvent. The crystal form may be formed by recrystn. out of solution The crystal form obtained in this way have different m.p., infra red spectrum and X-ray diffraction patterns from previously known forms "B-type" and "H-Type" of the compound

IT **105816-04-4**

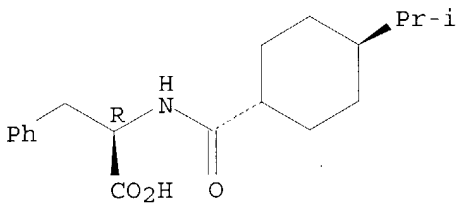
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(stable **crystal** form of N-trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine)

RN 105816-04-4 CAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 15 OF 35 USPATFULL on STN

AN 2003:325267 USPATFULL

TI Methods for producing nateglinide B-type **crystals**

IN Sumikawa, Michito, Yokkaichi-Shi, JAPAN
Maruo, Makoto, Yokkaichi-Shi, JAPAN
Miyazaki, Kazuo, Yokkaichi-Shi, JAPAN
Nishina, Shigehiro, Yokkaichi-Shi, JAPAN
Matsuzawa, Yukiko, Yokkaichi-Shi, JAPAN

PA AJINOMOTO CO. INC, Tokyo, JAPAN (non-U.S. corporation)

PI US 2003229249 A1 20031211

AI US 2003-421888 A1 20030424 (10)

RLI Continuation of Ser. No. WO 2001-JP9293, filed on 23 Oct 2001, UNKNOWN

PRAI JP 2000-324375 20001024

DT Utility

FS APPLICATION

LREP OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C., 1940 DUKE STREET, ALEXANDRIA, VA, 22314

CLMN Number of Claims: 9

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 191

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

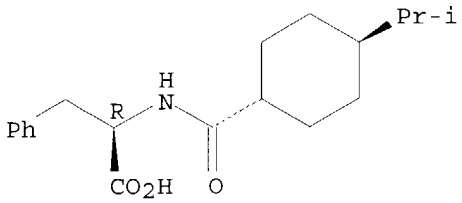
AB A method for producing B-type **crystals** of nateglinide substantially free of H-type **crystals** is provided, which comprises drying solvated wet **crystals** of nateglinide at a low temperature until no solvent remains and making a **crystal** conversion thereof. According to this method, B-type **crystals** of nateglinide can be produced at an industrial scale without allowing other forms of the **crystalline** polymorphism to coexist.

IT **105816-04-4P**, Nateglinide
(industrial process for producing B-form nateglinide crystals)

RN 105816-04-4 USPATFULL

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

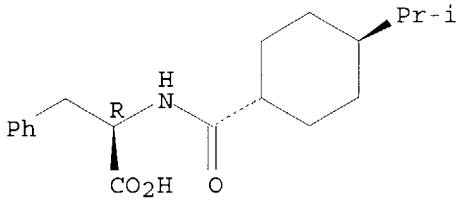


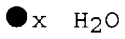
IT **173653-89-9**
(industrial process for producing B-form nateglinide crystals)

RN 173653-89-9 USPATFULL

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, hydrate (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).





L15 ANSWER 16 OF 35 USPATFULL on STN

AN 2003:232615 USPATFULL

TI Method of treating metabolic disorders, especially diabetes, or a disease or condition associated with diabetes

IN Gatlin, Marjorie Regan, Hoboken, NJ, UNITED STATES
Ball, Michele Ann, Morris Plains, NJ, UNITED STATES
Mannion, Richard Owen, Mount Arlington, NJ, UNITED STATES
Karnachi, Anees Abdulquadar, Hillsborough, NJ, UNITED STATES
Guitard, Christiane, Hagenheim, FRANCE
Allison, Malcolm, Basel, SWITZERLAND

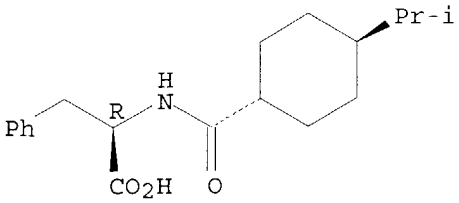
PI US 2003162816 A1 20030828

AI US 2003-345908 A1 20030116 (10)

RLI Continuation of Ser. No. US 2000-663264, filed on 15 Sep 2000, PENDING
PRAI GB 2000-21055 20000826
US 2000-304196P 20000407 (60)
US 2000-240918P 20000309 (60)
US 1999-240911P 19990917 (60)
DT Utility
FS APPLICATION
LREP THOMAS HOXIE, NOVARTIS, CORPORATE INTELLECTUAL PROPERTY, ONE HEALTH PLAZA 430/2, EAST HANOVER, NJ, 07936-1080
CLMN Number of Claims: 41
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2226
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to a combination, such as a combined preparation or pharmaceutical composition, respectively, which comprises nateglinide (I) ##STR1##

or repaglinide and at least one other antidiabetic compound selected from the group consisting of thiazolidinedione derivatives (glitazones), sulfonyl urea derivatives and metformin for simultaneous, separate or sequential use in the prevention, delay of progression or treatment of diseases, especially metabolic disorders and in particular type 2 diabetes and diseases and conditions associated with diabetes; to a composition, respectively, which comprises nateglinide and a pharmaceutically acceptable carrier and to a process of making such composition; the use of such combination or composition for the preparation of a medicament for the prevention, delay of progression or treatment of metabolic disorders; a method of prevention, delay of progression or treatment of diseases in warm-blooded animals; the use of such combination or composition for the cosmetic treatment of a mammal in order to effect a cosmetically beneficial loss of body weight; and to a method of improving the bodily appearance of a warm-blooded animal.
IT **105816-04-4**, Nateglinide
(pharmaceuticals containing nateglinide or repaglinide for treating diabetes or conditions associated with diabetes)
RN 105816-04-4 USPATFULL
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 17 OF 35 USPATFULL on STN
AN 2003:93574 USPATFULL
TI Amino acid complexes of C-aryl glucosides for treatment of diabetes and method
IN Gougoutas, Jack Z., Princeton, NJ, UNITED STATES
PI US 2003064935 A1 20030403
US 6774112 B2 20040810
AI US 2002-117914 A1 20020408 (10)

PRAI US 2001-283097P 20010411 (60)
DT Utility
FS APPLICATION
LREP STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1995
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB **Crystalline** complexes are obtained from a 1:1 or 2:1 mixtures of either the (D) or (L) enantiomer of natural amino acids and compounds of formula ##STR1##

wherein

R.sup.1, R.sup.2 and R.sup.2a are independently hydrogen, OH, OR.sup.5, alkyl, --OCHF.sub.2, --OCF.sub.3, --SR.sup.5a or halogen;

R.sup.3 and R.sup.4 are independently hydrogen, OH, OR.sup.5b, alkyl, cycloalkyl, CF.sub.3, --OCHF.sub.2, --OCF.sub.3, halogen, --CONR.sup.6R.sup.6a, --CO.sub.2R.sup.5c, --CO.sub.2H, --COR.sup.6b, --CH(OH)R.sup.6c, --CH(OR.sup.5d)R.sup.6d, --CN, --NHCOR.sup.5e, --NHSO.sub.2R.sup.5f, --NHSO.sub.2Aryl, --SR.sup.5g, --SOR.sup.5h, --SO.sub.2R.sup.5i, or a five, six or seven membered heterocycle which may contain 1 to 4 heteroatoms in the ring which are N, O, S, SO, and/or SO.sub.2, or R.sup.3 and R.sup.4 together with the carbons to which they are attached form an annelated five, six or seven membered carbocycle or heterocycle which may contain 1 to 4 heteroatoms in the ring which are N, O, S, SO, and/or SO.sub.2;

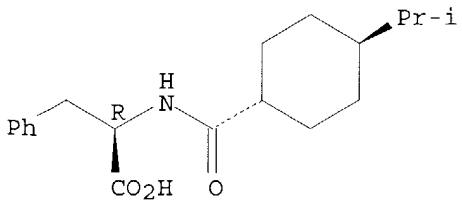
R.sup.5, R.sup.5a, R.sup.5b, R.sup.5c, R.sup.5d, R.sup.5e, R.sup.5f, R.sup.5g, R.sup.5h and R.sup.5i are independently alkyl;

R.sup.6, R.sup.6a, R.sup.6b, R.sup.6c and R.sup.6d are independently hydrogen, alkyl, aryl, alkylaryl or cycloalkyl, or R.sup.6 and R.sup.6a together with the nitrogen to which they are attached form an annelated five, six or seven membered heterocycle which may contain 1 to 4 heteroatoms in the ring which are N, O, S, SO, and/or SO.sub.2.

A method is also provided for treating diabetes and related diseases employing an SGLT2 inhibiting amount of the above complex alone or in combination with another antidiabetic agent or other therapeutic agent.

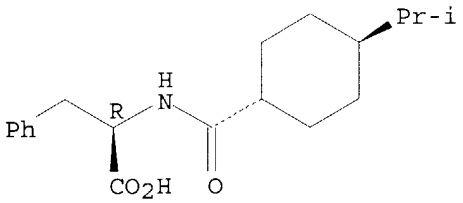
IT **105816-04-4**, Nateglinide
(preparation of amino acid/C-aryl glucoside complexes for treatment of diabetes and related diseases)
RN 105816-04-4 USPATFULL
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 18 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:697592 CAPLUS
DN 140:187130
TI Study on stability of nateglinide **polymorphism**
AU Li, Gang; Xu, Qun Wei; Mo, Xiang Yin; Chen, Jia Ying; Su, Guo Qiang
CS Chemistry and Physics Centralaboratory, Nanjing Normal University, Nanjing, 210097, Peop. Rep. China
SO Chinese Chemical Letters (2003), 14(7), 730-733
CODEN: CCLEE7; ISSN: 1001-8417
PB Chinese Chemical Society
DT Journal
LA English
AB The stability of three forms of nateglinide, especially, S-form and H-form, was determined The S-form was a new crystal structure of nateglinide. Three forms of nateglinide were treated under different conditions such as in various temps., humidity, light, etc. Anal. of their crystal structures was performed by x-ray powder diffraction and their particle shapes were observed with scanning electron microscope. The results indicated that the stability of S-form of nateglinide is the best among the three forms and their particle shapes are quite different. The S-form is the sheet structure of layer upon layer, H-form looks like a hank of silk lines and the B-form is of clubbed shape.
IT **105816-04-4**, Nateglinide
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stability of nateglinide **polymorphs**)
RN 105816-04-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 19 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:146027 CAPLUS
DN 139:235199
TI Study on stability of nateglinide **polymorphism**
AU Li, Gang; Xu, Qun-Wei; Mo, Xiang-Yin; Chen, Jia-Ying; Su, Guo-Qiang
CS Testing & Analysis Center, Nanjing Normal University, Nanjing, 210097, Peop. Rep. China
SO Huaxue Xuebao (2003), 61(2), 291-294
CODEN: HHHPA4; ISSN: 0567-7351
PB Kexue Chubanshe
DT Journal
LA Chinese
AB A study has been made on the stability of three forms of nateglinide treated in different conditions, such as temperature, humidity, irradiation and so

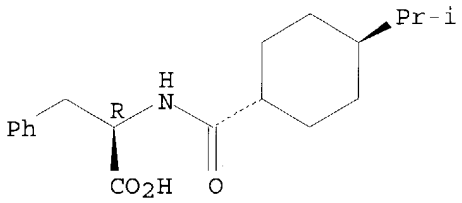
on. Anal. of the crystal structure was performed by x-ray powder diffraction. Their particle shapes were observed in scan electron microscope. The results show that the stability of S-form of nateglinide is the best among the three forms.

IT **105816-04-4**, Nateglinide
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stability of nateglinide **polymorphism**)

RN 105816-04-4 CAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:813874 CAPLUS

DN 137:311199

TI Amino acid complexes of C-aryl glucosides for treatment of diabetes

IN Gougoutas, Jack Z.

PA Bristol-Myers Squibb Company, USA

SO PCT Int. Appl., 80 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002083066	A2	20021024	WO 2002-US11066	20020408
	WO 2002083066	A3	20030306		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003064935	A1	20030403	US 2002-117914	20020408
	US 6774112	B2	20040810		
	EP 1385856	A2	20040204	EP 2002-723801	20020408
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2001-283097P	P	20010411		
	WO 2002-US11066	W	20020408		

OS MARPAT 137:311199

AB Crystalline complexes are obtained from 1:1 or 2:1 mixts. of either the (D) or (L) enantiomer of natural amino acids and compds. of formula I [R1, R2, R2a = H, OH, OR5, alkyl, OCHF2, OCF3, SR5a, halogen; R3, R4 = H, OH, OR5b,

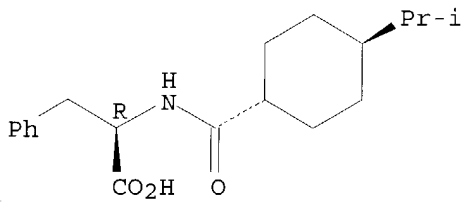
alkyl, cycloalkyl, CF3, OCHF2, OCF3, halogen, CONR6R6a, CO2R5c, CO2H, COR6b, CH(OH)R6c, CH(OR5d)R6d, CN, NHCOR5e, NHSO2R5f, NHSO2-aryl, SR5g, SOR5h, SO2R5i, or a five, six or seven membered heterocycle which may contain 1 to 4 heteroatoms (N, O, S, SO, and/or SO2), or R3 and R4 together with the carbons to which they are attached form an annelated five, six or seven membered carbocycle or heterocycle which may contain 1 to 4 heteroatoms in the ring; R5, R5a-R5i are independently alkyl; R6, R6a-R6d are independently H, alkyl, aryl, alkylaryl or cycloalkyl, or NR6R6a form an annelated five, six or seven membered heterocycle which may contain 1 to 4 heteroatoms in the ring]. A method is also provided for treating diabetes and related diseases employing an SGLT2 (sodium dependent glucose transporters found in the intestine and kidney) inhibiting amount of the above complex alone or in combination with another antidiabetic agent or other therapeutic agent. Thus, I (R1 = 4-Me, R4 = 4-OCHF2, R2, R2a, R3 = H) was prepared by a multistep procedure starting from o-toluic acid, anisole, 2,3,4,6-tetra-O-benzyl-β-D-glucolactone, and CHF2Cl and treated with L-phenylalanine to form the crystalline 1:1 complex.

IT **105816-04-4**, Nateglinide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of amino acid/C-aryl glucoside complexes for treatment of diabetes and related diseases)

RN 105816-04-4 CAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 21 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:391524 CAPLUS
DN 136:374894
TI . Nateglinide-containing hydrophilic drug preparations
IN Ninomiya, Nobutaka; Makino, Chisato; Yabuki, Akira
PA Ajinomoto Co., Inc., Japan
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002040010	A1	20020523	WO 2001-JP9292	20011023
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,				

BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	AU 2001096000	A5	20020527	AU 2001-96000	20011023
	BR 2001014897	A	20030812	BR 2001-14897	20011023
	EP 1334721	A1	20030813	EP 2001-976818	20011023
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2004029968	A1	20040212	US 2003-420886	20030423
PRAI	JP 2000-324374	A	20001024		
	WO 2001-JP9292	W	20011023		

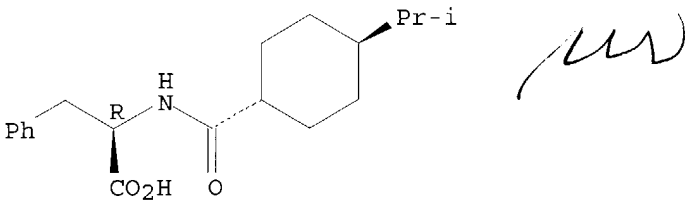
AB Hydrophilic drug prepns. contain nateglinide B crystals useful as a hypoglycemic agent as the active ingredient which comprises a hydrophilic substance selected from the group consisting of hydrophilic polymers, surfactants, sugars, sugar alcs. and salts, and thus have a contact angle of the preparation surface to water of 111° or less. These prepns., which are rapid release prepns. having high elution properties, can be easily produced.

IT **105816-04-4**, Nateglinide
RL: BCP (Biochemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(hypoglycemic hydrophilic drug prepns. containing)

RN 105816-04-4 CAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 22 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:332157 CAPLUS

DN 136:340998

TI Process for producing B-form nateglinide **crystals**

IN Sumikawa, Michito; Maruo, Makoto; Miyazaki, Kazuo; Nishina, Shigehiro; Matsuzawa, Yukiko

PA Ajinomoto Co., Inc., Japan

SO PCT Int. Appl., 9 pp.
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002034713	A1	20020502	WO 2001-JP9293	20011023
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	AU 2001096001	A5	20020506	AU 2001-96001	20011023
	EP 1334964	A1	20030813	EP 2001-976819	20011023
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001014846	A	20040225	BR 2001-14846	20011023
	US 2003229249	A1	20031211	US 2003-421888	20030424
PRAI	JP 2000-324375	A	20001024		
	WO 2001-JP9293	W	20011023		

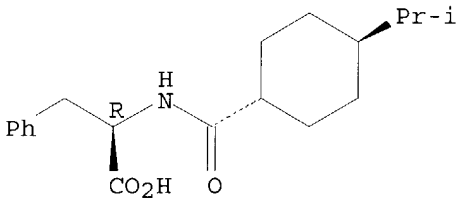
AB A process for producing B-form nateglinide crystals containing substantially no H-form crystals comprises the steps of drying wet crystals of a nateglinide solvate at a low temperature until the solvent disappears and then causing them to undergo a crystal transition. Nateglinide is a known antidiabetic. By this process, B-form nateglinide crystals can be produced on an industrial scale.

IT **105816-04-4P**, Nateglinide
RL: PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(industrial process for producing B-form nateglinide **crystals**
)

RN 105816-04-4 CAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

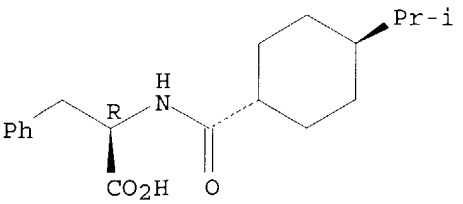


IT **173653-89-9**
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(industrial process for producing B-form nateglinide **crystals**
)

RN 173653-89-9 CAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, hydrate (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



●x H_2O

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

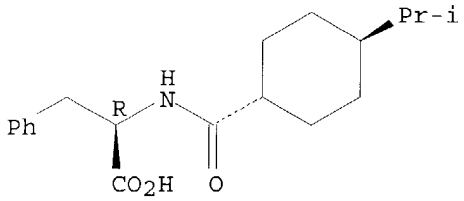
L15 ANSWER 23 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:314896 CAPLUS
DN 136:325825
TI Process for producing nateglinide **crystals**
IN Takahashi, Daisuke; Nishi, Seiichi; Takahashi, Satoji
PA Ajinomoto Co., Inc., Japan
SO PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002032854	A1	20020425	WO 2001-JP9069	20011016
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001094265	A5	20020429	AU 2001-94265	20011016
	EP 1334963	A1	20030813	EP 2001-974875	20011016
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001014729	A	20031014	BR 2001-14729	20011016
	US 2004030182	A1	20040212	US 2003-418105	20030418
PRAI	JP 2000-317604	A	20001018		
	WO 2001-JP9069	W	20011016		

AB A process for producing nateglinide crystals comprises reacting trans-4-isopropylcyclohexylcarbonyl chloride with D-phenylalanine in a mixed solvent consisting of a ketone solvent and water in the presence of an alkali to obtain a reaction mixture containing nateglinide, adding an acid to the reaction mixture to make it acidic, and regulating (a) the temperature to 58° to 72° and (b) and the ketone solvent concentration to > 8 weight% and < 22 weight%, to conduct crystallization Nateglinide is a known antidiabetic.
The process is an industrially advantageous method for crystallizing nateglinide.

IT **105816-04-4P**, Nateglinide
RL: IMF (Industrial manufacture); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for producing nateglinide **crystals**)
RN 105816-04-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

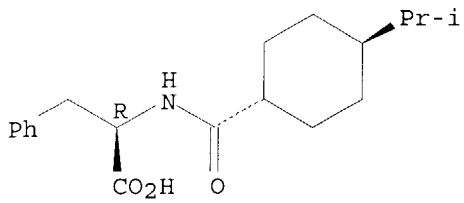
Absolute stereochemistry. Rotation (-).



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 24 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:686087 CAPLUS
DN 140:292376
TI Study on the **crystal** types of nateglinide
AU Sun, Piaoyang; Gou, Shaohua; Ma, Yonglin
CS State Key Laboratory of Coordination Chemistry, Nanjing University, Nanjing, 210093, Peop. Rep. China
SO Huaxue Yanjiu Yu Yingyong (2002), 14(4), 457-458, C3
CODEN: HYYIFM; ISSN: 1004-1656
PB Huaxue Yanjiu Yu Yingyong Bianjibu
DT Journal
LA Chinese
AB N-(trans-4-methylethylcyclohexylcarbonyl)-D-phenylalanine, nateglinide, is an effective drug to decrease blood sugar, which is under clin. trials in China. This compound has been reported to have two crystal types, one of which is more suitable to prepare the drug. The nateglide with different crystal types was prepared Their m.ps., TGA-DTA and DSC spectral data, LR and X-ray powder diffraction spectra of all samples were studied with different crystal types. A new crystal type that has not been reported in the literature was discovered. The method for controlling the crystal type was also presented.
IT **105816-04-4**, Nateglinide
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**polymorphism**; **polymorphism** of nateglinide)
RN 105816-04-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

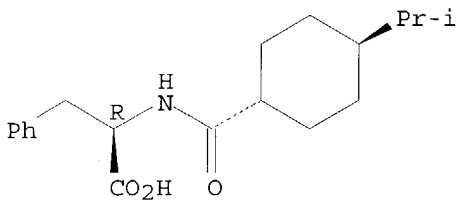
Absolute stereochemistry. Rotation (-).



L15 ANSWER 25 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:811385 CAPLUS
DN 139:12440
TI Identification of nateglinide and its **crystal** forms in nateglinide tablets using IR Spectra subtraction techniques
AU Lin, Kejiang; Chen, Wei; Tang, Weiguo; You, Qidong

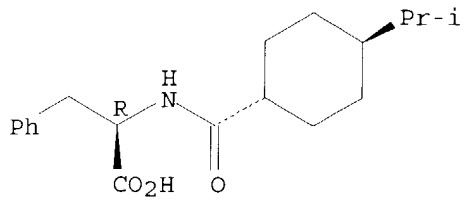
CS Department of Medicinal Chemistry, China Pharmaceutical University, Nanjing, 21009, Peop. Rep. China
SO Zhongguo Yaoke Daxue Xuebao (2002), 33(2), 124-126
CODEN: ZHYXE9; ISSN: 1000-5048
PB Zhongguo Yaoke Daxue
DT Journal
LA Chinese
AB The innovational identification method of IR (eliminated method) for detection of the crystal form of nateglinide in prepns. was presented. The IR spectrum by spectra subtraction techniques was obtained by subtracting IR spectrum after adding small volume of solvent to eliminate nateglinide from the spectrum of nateglinide tablets' KBr disk to identify the crystal form of nateglinide. The method (eliminated method) was useful in identification of the nateglinide crystal form in prepns.
IT **105816-04-4**, Nateglinide
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(identification of nateglinide and its **crystal** forms in nateglinide tablets using IR spectra subtraction techniques)
RN 105816-04-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



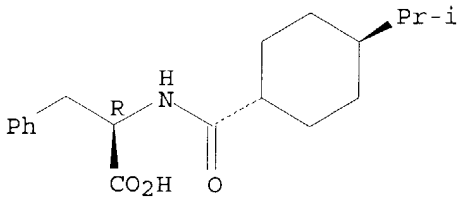
L15 ANSWER 26 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:609152 CAPLUS
DN 138:254901
TI a new synthesis method of nateglinide as antidiabetic drug
AU Wang, Dun; Liang, Yiheng; Gong, Ping; Zhao, Yanfang
CS School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China
SO Zhongguo Yaowu Huaxue Zazhi (2002), 12(2), 94-96
CODEN: ZYHZEF; ISSN: 1005-0108
PB Zhongguo Yaowu Huaxue Zazhi Bianjibu
DT Journal
LA Chinese
OS CASREACT 138:254901
AB A new antidiabetic drug-nateglinide was synthesized from isopropylbenzene by Friedel-Crafts reaction, chloroform reaction, catalytic hydrogenation to obtain trans-4-isopropylhexanecarboxylic acid, acylation of D-phenylalanine Et ester, hydrolysis to obtain nateglinide B-type crystal, and crystal-conversion. The total yield was 9.8%.
IT **105816-04-4P**, Nateglinide
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of nateglinide as antidiabetic drug)
RN 105816-04-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



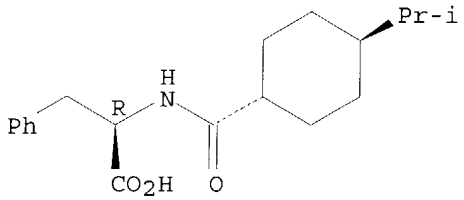
L15 ANSWER 27 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
AN 2002:234892 CAPLUS
DN 137:39555
TI Detection of **crystal polymorphs** of nateglinide by DSC
AU Lin, Kejiang; Chen, Wei; You, Qidong
CS China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SO Yaoxue Xuebao (2002), 37(1), 46-49
CODEN: YHHPAL; ISSN: 0513-4870
PB Yaoxue Xuebao Bianjibu
DT Journal
LA Chinese
AB The differential scanning calorimetric (DSC) methodol. for controlling the crystal-type B form of nateglinide was presented. Pure fine powder of crystal-type B and H of nateglinide dried with P2O5 as desiccant at 80° in vacuum for 4 h was measured dQ/dT by DSC at heating rate of 10° min-1 and temperature between 100° and 200° to calculate the enthalpy ΔHB and ΔHH. Uniform mixts. of crystal-type B and H of dried fine powder of nateglinide in different proportions were accurately weighed. The enthalpy of the mixts. was measured by DSC as above to calculate the enthalpy (ΠΔH). Using B% as X, ΠΔH as parameters, the regression equation was obtained. Based on this equation, the unknown composition of mixed crystal was evaluated by yδH values. The method was used to control the limitation of crystal-type B of nateglinide by the HδH value of mixture of known composition as reference The results measured from different labs. showed that the repeatability was 0.61% and recoveries were 86.2-127% when the amount of crystal-type B was between 0-15%. This method can be used to evaluate the crystal-type B composition of nateglinide.
IT **105816-04-4**, Nateglinide
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); PROC (Process)
(detection of **crystal polymorphs** of nateglinide by DSC)
RN 105816-04-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 28 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:762699 CAPLUS
DN 140:64875
TI Study of nateglinide **polymorphism**
AU Li, Gang; Xu, Qunwei; Yao, Jie; Su, Guoqiang; Wang, Fang
CS Chemistry and Physics Central- laboratory, Nanjing Normal University, Nanjing, 210097, Peop. Rep. China
SO Huagong Shikan (2002), 16(7), 17-18
CODEN: HUSHFT; ISSN: 1002-154X
PB Huagong Shikan Zazhishe
DT Journal
LA Chinese
AB The crystal structure of nateglinide called an S form determined by an x-ray powder diffraction method. The pattern, data, and crystal size were obtained. The m.p. was determined by DSC as 172.04°.
IT **105816-04-4**, Nateglinide
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nateglinide **polymorphism**)
RN 105816-04-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 29 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:283772 CAPLUS
DN 134:285620
TI Method of treating metabolic disorders with nateglinide
IN Gatlin, Marjorie Regan; Pongowski, Michele; Dunning, Beth
PA Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001026639	A2	20010419	WO 2000-EP9816	20001006
	WO 2001026639	A3	20020110		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1218015 A2 20020703 EP 2000-972695 20001006

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRAI US 1999-415307 A 19991008

US 1999-415308 A 19991008

WO 2000-EP9816 W 20001006

AB The invention relates to a combination which comprises nateglinide and (a) an antidiabetic phenylacetic acid derivative or (b) acarbose for simultaneous, sep. or sequential use, in particular in the treatment of diseases, especially metabolic disorders; to a method of prevention, delay of progression or treatment of metabolic disorders, more especially diabetes, or a disease or condition associated with diabetes, and to a method of improving the bodily appearance of a warm-blooded animal.

IT **105816-04-4**, Nateglinide

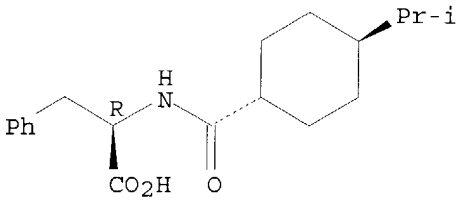
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(treating metabolic disorders with nateglinide)

RN 105816-04-4 CAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 30 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:130037 CAPLUS

DN 137:325603

TI Synthesis of Nateglinide

AU Zhu, Xue-yan; Peng, Ka; Wang, Xiao-qin; Yang, Li-ping

CS Dep. Chem., East China Normal Univ., Shanghai, 200062, Peop. Rep. China

SO Hecheng Huaxue (2001), 9(6), 537-540

CODEN: HEHUE2; ISSN: 1005-1511

PB Hecheng Huaxue Bianjibu

DT Journal

LA Chinese

OS CASREACT 137:325603

AB Title compound, a new antidiabetes medicine, was synthesized from iso-propylbenzene in seven steps, giving the product with overall yield 22%.

IT **105816-04-4DP**, Nateglinide, B **crystal** type

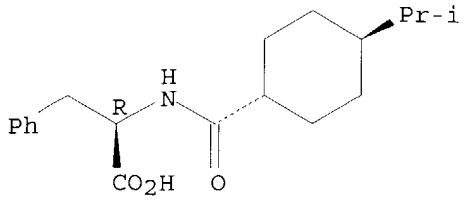
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and **crystalline** forms of)

RN 105816-04-4 CAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

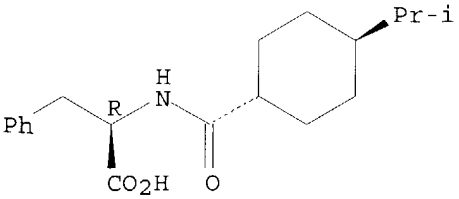
Absolute stereochemistry. Rotation (-).



RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of Nateglinide

L15 ANSWER 31 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
AN 2001:625224 CAPLUS
DN 136:348527
TI New **crystal** form of nateglinide
AU Li, Gang; Su, Guoqiang; Xu, Qunwei; Zhu, Chongquan
CS Chemistry and Physics Central Laboratory, Nanjing Normal University, Nanjing, 210097, Peop. Rep. China
SO Yaoxue Xuebao (2001), 36(7), 532-534
CODEN: YHHPAL; ISSN: 0513-4870
PB Yaoxue Xuebao Bianjibu
DT Journal
LA Chinese
AB The S form crystals of nateglinide [N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine] were studied by XRD, IR, elemental anal., and differential scan calorimetry. The S-form nateglinide crystal was different from the H-form or B-form. The m.p. was 172.04°. The results showed that the S-form nateglinide was a new crystal form.
IT **105816-04-4**, Nateglinide
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new **crystal** form of nateglinide)
RN 105816-04-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

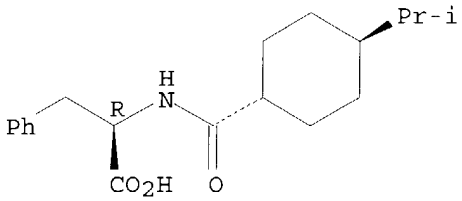
Absolute stereochemistry. Rotation (-).



L15 ANSWER 32 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:844448 CAPLUS
DN 136:159110
TI A new **crystal** structure in nateglinide found by X-ray powder diffraction
AU Li, Gang; Su, Guo-qiang; Xu, Qun-wei
CS Center for Analysis & Measurement, Nanjing Normal University, Nanjing, 210097, Peop. Rep. China
SO Yaowu Fenxi Zazhi (2001), 21(5), 342-344

CODEN: YFZADL; ISSN: 0254-1793
PB Yaowu Fenxi Zazhi Bianji Weiyuanhui
DT Journal
LA Chinese
AB A new crystal structure being assigned as S-form was found in nateglinide. The x-ray pattern and data were given and the m.p. was determined Phase anal. was carried out by x-ray powder diffraction; the m.ps. were determined by DSC. S-form nateglinide was different from the H or B crystal form. The m.p. was 172.04°. S-form nateglinide was a new crystal form. X-ray powder diffraction anal. was one of the most effective methods for phase structure characterization.
IT **105816-04-4**, Nateglinide
RL: PRP (Properties)
(**crystal** structure of)
RN 105816-04-4 CAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

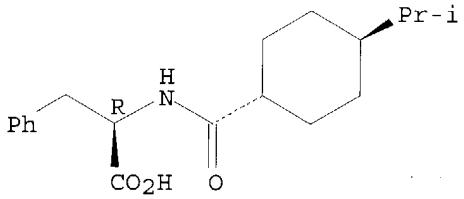


L15 ANSWER 33 OF 35 USPATFULL on STN
AN 96:9521 USPATFULL
TI **Crystals** of N-(trans-4-isopropylcyclohexycarbonyl)-D-phenylalanine and methods for preparing them
IN Sumikawa, Michito, Kawasaki, Japan
Koguchi, Yoshihito, Kawasaki, Japan
Ohgane, Takao, Kawasaki, Japan
Irie, Yasuo, Kawasaki, Japan
Takahashi, Satoji, Yottukaichi, Japan
PA Ajinomoto Co., Inc., Tokyo, Japan (non-U.S. corporation)
PI US 5488150 19960130
AI US 1993-166144 19931214 (8)
RLI Continuation of Ser. No. US 1992-921224, filed on 29 Jul 1992, now abandoned
PRAI JP 1991-189696 19910730
JP 1991-199453 19910808
DT Utility
FS Granted
EXNAM Primary Examiner: Henley, III, Raymond; Assistant Examiner: MacMillan, Keith
LREP Oblon, Spivak, McClelland, Maier, & Neustadt
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 528
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Stable **crystals** of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine may be produced by treating this compound with a solvent at a temperature of at least 10° C. and forming **crystals** in the solvent at a temperature of at least 10° C. For example,

crystals may be formed by **crystallization** out of solution, or may be formed from solid particles of the compound suspended in a solvent. **Crystals** formed in this way have different melting point, infra red spectrum and X-ray diffraction patterns from previously known forms of the compound and have enhanced processability, eg. stability to grinding.

IT **105816-04-4P**
(crystals, stable, preparation of)
RN 105816-04-4 USPATFULL
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 34 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
AN 1995:964992 CAPLUS
DN 124:155974
TI **Crystals** of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine and methods for preparing them
IN Sumikawa, Michito; Koguchi, Yoshihito; Ohgane, Takao; Irie, Yasuo; Takahashi, Satoji
PA Ajinomoto Co., Inc., Japan
SO U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 166,144.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5463116	A	19951031	US 1994-190460	19940202
	US 5488150	A	19960130	US 1993-166144	19931214
	CA 2114678	AA	19950802	CA 1994-2114678	19940201
	CA 2114678	C	19990427		
PRAI	JP 1991-189696	A	19910730		
	JP 1991-199453	A	19910808		
	US 1992-921224	B1	19920729		
	US 1993-166144	A2	19931214		

AB Stable crystals of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine for pharmaceutical formulation may be produced by treating this compound with a solvent at a temperature of at least 10° and forming crystals in the solvent at a temperature of at least 10°. For example, crystals may be formed by crystallization out of solution, or may be formed from solid particles of the compound suspended in a solvent. Crystals formed in this way have different m.p., IR spectrum and X-ray diffraction patterns from previously known forms of the compound and have enhanced processability, e.g., stability to grinding.

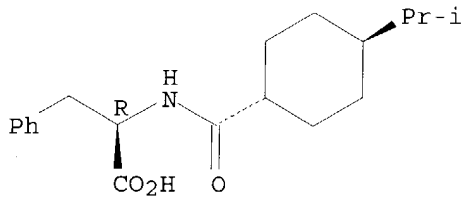
IT **105816-04-4**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(**crystallization** of (isopropylcyclohexylcarbonyl)phenylalanine for enhanced stability to grinding)

RN 105816-04-4 CAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **173653-89-9**

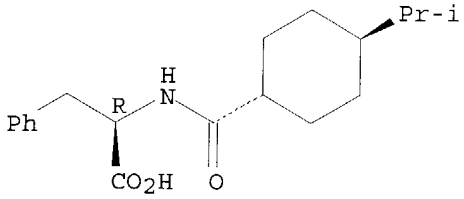
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(**crystallization** of (isopropylcyclohexylcarbonyl)phenylalanine for enhanced stability to grinding)

RN 173653-89-9 CAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, hydrate (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



●x H_2O

L15 ANSWER 35 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:261002 CAPLUS

DN 118:261002

TI Stable **crystals** of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine

IN Sumikawa, Michito; Koguchi, Yoshihito; Ohgane, Takao; Irie, Yasuo; Takahashi, Satoji

PA Ajinomoto Co., Inc., Japan

SO Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 526171	A2	19930203	EP 1992-306895	19920729
	EP 526171	A3	19930505		

	EP 526171	B1	19970305		
	R: AT, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
	JP 05208943	A2	19930820	JP 1992-202686	19920729
	JP 2508949	B2	19960619		
	AT 149483	E	19970315	AT 1992-306895	19920729
	ES 2100291	T3	19970616	ES 1992-306895	19920729
	CA 2114678	AA	19950802	CA 1994-2114678	19940201
	CA 2114678	C	19990427		
PRAI	JP 1991-189696	A	19910730		
	JP 1991-199453	A	19910808		

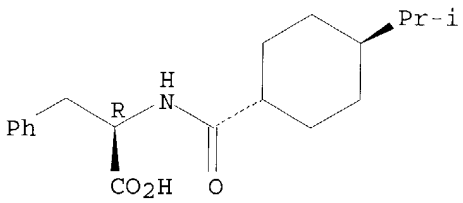
AB Stable H-type crystals of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (I) are obtained by treating I with a solvent, at >10°. A solution of 5 g I in 20 mL acetone was added to a stirred mixture of 40 mL acetone and 60 mL water, at 25° to precipitate H-type crystals. The crystals have different m.p., IR spectrum and x-ray diffraction patterns from known forms of I and are not converted to other forms when ground.

IT **105816-04-4P**
RL: PREP (Preparation)
(**crystals**, stable, preparation of)

RN 105816-04-4 CAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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L43 NOT FOUND

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L2 362002 SEA FILE=WPIDS ABB=ON PLU=ON CRYS?
L3 16 SEA FILE=WPIDS ABB=ON PLU=ON L1 AND L2

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L3 ANSWER 1 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2004-594140 [57] WPIDS
CR 2004-108803 [11]; 2004-180282 [17]
DNC C2004-216153
TI New **crystalline nateglinide** form-U useful to reduce blood glucose level and to treat type-II diabetes.
DC B05
IN FRENKEL, G; GOME, B; WIZEL, S
PA (TEVA-N) TEVA PHARM IND LTD; (TEVA-N) TEVA PHARM USA INC
CYC 107
PI WO 2004067496 A1 20040812 (200457)* EN 124
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
ADT WO 2004067496 A1 WO 2004-US839 20040113
PRAI US 2003-746697 20031224; US 2003-442109P 20030123;
US 2003-449791P 20030224; US 2003-479016P 20030616;
US 2003-622905 20030718; WO 2003-US22375 20030718;
US 2003-693166 20031023
AB WO2004067496 A UPAB: 20040907
NOVELTY - **Crystalline nateglinide** form-U (I)
substantially free of a peak at 3.8 plus or minus 0.2 theta is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for
(1) the preparation of (I); and
(2) a process for purifying (I).
ACTIVITY - Antidiabetic.
No biological data given.
MECHANISM OF ACTION - None given.
USE - (I) is useful to lower blood sugar level and to treat type II diabetes (claimed).
ADVANTAGE - (I) has improved pharmaceutical characteristics such as targeted release profile.
Dwg.0/69
TECH UPTX: 20040907
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation (Claimed): Preparation

of (I) comprises
(a) either preparing a solution of **nateglinide** in ethyl acetate at about 40-45 degrees C and adding in any order a 5-12C aliphatic hydrocarbon having about 5 degrees C as an anti-solvent to precipitate **nateglinide**; or
(b) preparing a solution of **nateglinide** in ethylacetate, seeding the solution with **nateglinide crystals** and recovering the **crystalline** form as a precipitate; or
(c) preparing a container holding a solution of **nateglinide** in ethyl acetate, adding 5-12C hydrocarbon to the container holding the solution and recovering the **crystalline** form as a precipitate; or
(d) preparing a solution of **nateglinide** in a mixture of water and ethyl acetate, combining the solution with an anti-solvent and recovering the **crystalline nateglinide** as a precipitate.
Purification of (I) comprises **crystallizing** the **crystalline nateglinide** from a solution in the presence of water resulting in the **crystalline** form being 99% pure as area percentage high performance liquid chromatography.
Preferred Components: (I) has a XRPD pattern with peaks at about 4.7, 7.4, 13.8 and 17.0+/-0.2 and a FTIR spectrum with peaks at about 3350, 1701, 1646 and 1291 cm-1.
Preferred Process: The antisolvent is heptane. The volume of ethyl acetate is 3-11 (preferably 4-6) ml/g compared to weight of the **nateglinide.** The solution is seeded with the same **crystalline** form. The preparation further comprises cooling before or after seeding and seeding before precipitation. (I) obtained is free of other **crystalline** forms by weight. The hydrocarbon is a 5-8C hydrocarbon (preferably heptane) and is added in such a manner to avoid precipitation upon addition. The precipitation is carried out in the presence of water. The recovering of (I) is by filtering the precipitate. The preparation also comprises preparing a solution of **nateglinide** in ethyl acetate at 25-50 degrees C at an ethyl acetate/ **nateglinide** ratio of about 3 -1 ml/g, seeding the solution with the same **crystalline nateglinide** at about 10-35 degrees C, stirring the seeded solution, cooling the seeded solution at a rate of about 1-10 degrees C per hour to a temperature of about (-)10-10 degrees C, filtering the **crystalline nateglinide** as a precipitate and drying the precipitate. The ethyl acetate is mixed with water at about 2-10% water as percentage of milliliters of water to grams of **nateglinide.** The anti-solvent is a 5-12C hydrocarbon (preferably heptane). In the purification process the rest of the solution is comprised of ethyl acetate.

L3 ANSWER 2 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2004-269196 [25] WPIDS
DNC C2004-104807
TI New **crystalline** form of **nateglinide** useful to treat diabetes and to stimulate insulin secretion from pancreas.
DC B05
IN KADABOINA, R; POLAVARAPU, S; REGURI, B R
PA (REDD-N) REDDY'S LAB LTD
CYC 105
PI WO 2004020396 A1 20040311 (200425)* EN 29
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH

PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

US 2004077725 A1 20040422 (200428)

ADT WO 2004020396 A1 WO 2003-US26880 20030827; US 2004077725 A1 US 2003-649380 20030827

PRAI IN 2002-CH631 20020828

AB WO2004020396 A UPAB: 20040525

NOVELTY - **Crystalline** form X of **nateglinide** (I) is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for (1) a composition (B) comprising **nateglinide** as a solid, where at least 80% by weight of the solid is (I); and

(2) preparation of (I).

ACTIVITY - Antidiabetic.

MECHANISM OF ACTION - None given in the source material.

USE - (I) is useful to treat diabetes and also stimulates the secretion of insulin from pancreas.

Dwg.0/2

TECH UPTX: 20040418

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation (Claimed): Preparation of (I) comprises:

(a) providing a solution of **nateglinide** in an aromatic hydrocarbon solvent;

(b) cooling the solution until a precipitate is formed; and

(c) isolating (I).

Preferred Process: The starting **nateglinide** is **crystalline** form H and/or B. The hydrocarbon solvent is benzene, ethylbenzene and toluene (preferably xylene or ortho-xylene). The process further comprises heating the mixture of the starting material and hydrocarbon solvent at 40 degrees C - 130 degrees C (preferably 50 degrees C - 70 degrees C), drying the isolated precipitate and filtering the **nateglinide** solution before cooling. Cooling is carried out at 25 degrees C - 35 degreesC

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: (I) exhibits an X-ray diffraction pattern expressed in terms of 2 theta angles, that includes 5 or more peaks of 3.95+/-0.09, 4.89+/-0.09, 5.18+/-0.09, 6.78+/-0.09, 7.79+/-0.09, 10.32+/-0.09, 13.51+/-0.09, 14.00+/-0.09, 16.98+/-0.09, 17.94+/-0.09, 18.85+/-0.09, 19.17+/-0.09, 20.32+/-0.09, 21.12+/-0.09, 22.52+/-0.09, 23.76+/-0.09, 24.46+/-0.09, 27.36+/-0.09, 28.17+/-0.09, 30.88+/-0.09, 31.25+/-0.09, 32.61+/-0.09, and 41.65+/-0.09 degrees (particularly 3.95+/-0.09, 14.00+/-0.09, 16.98+/-0.09) against Lin (counts per second) and 2 theta angles. The X-ray diffraction pattern further includes 3.952, 14.039, 16.98, 20.325, 21.120, 17.942, 6.776, 13.515 and 18.853 degrees. (I) also exhibits an infrared absorption spectrum with absorption bands at about 3353 cm-1, 2937cm-1, 2868 cm-1, 1743 cm-1, 1646 cm-1, 1597 cm-1, 1445 cm-1, 1208 cm-1, 1190 cm-1, 1110 cm-1, 697 cm-1 and 607 cm-1 against T% and cm-1.

Preferred Composition: (B) comprises at least 90% (preferably 99%) by weight of (I) and at least 1% (preferably 5%) solid **nateglinide** is not its **crystalline** form. The solid **nateglinide** is substantially free of its **crystalline** forms B and H.

L3 ANSWER 3 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2004-180282 [17] WPIDS

CR 2004-108803 [11]; 2004-594140 [57]

DNC C2004-071244

TI New **crystalline** polymorphic forms of **nateglinide** useful for lowering the blood sugar level.

DC B05

IN DOLITZKY, B; GOME, B; GOZLAN, Y; SHAPIOR, E; YAHALOMI, R; SHAPIRO, E
PA (TEVA-N) TEVA PHARM IND LTD; (DOLI-I) DOLITZKY B; (GOME-I) GOME B; (GOZL-I) GOZLAN Y; (SHAP-I) SHAPIRO E; (YAHA-I) YAHALOMI R; (TEVA-N) TEVA PHARM USA INC
CYC 105
PI WO 2004009532 A1 20040129 (200417)* EN 130
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
US 2004116526 A1 20040617 (200440)
AU 2003253971 A1 20040209 (200450)
US 2004152782 A1 20040805 (200452)
ADT WO 2004009532 A1 WO 2003-US22375 20030718; US 2004116526 A1 Provisional US 2002-396904P 20020718, Provisional US 2002-413622P 20020925, Provisional US 2002-414199P 20020926, Provisional US 2002-423750P 20021105, Provisional US 2002-432093P 20021210, Provisional US 2002-432962P 20021212, Provisional US 2003-442109P 20030123, Provisional US 2003-449791P 20030224, Provisional US 2003-479016P 20030616, US 2003-623237 20030718; AU 2003253971 A1 AU 2003-253971 20030718; US 2004152782 A1 Provisional US 2002-393495P 20020703, Provisional US 2002-396904P 20020718, Provisional US 2002-413622P 20020925, Provisional US 2002-414199P 20020926, Provisional US 2002-423750P 20021105, Provisional US 2002-432093P 20021210, Provisional US 2002-432962P 20021212, Provisional US 2003-442109P 20030123, Provisional US 2003-449791P 20030224, US 2003-614266 20030703
FDT AU 2003253971 A1 Based on WO 2004009532
PRAI US 2003-614266 20030703; US 2002-396904P 20020718;
US 2002-413622P 20020925; US 2002-414199P 20020926;
US 2002-423750P 20021105; US 2002-432093P 20021210;
US 2002-432962P 20021212; US 2003-442109P 20030123;
US 2003-449791P 20030224; US 2003-479016P 20030616;
US 2003-623237 20030718; US 2002-393495P 20020703
AB WO2004009532 A UPAB: 20040907
NOVELTY - 26 **Crystalline nateglinide** forms as characterized by XRPD patterns, DSC thermograms and FTIR spectra, fully described in the specification, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the preparation of the **crystalline** forms of **nateglinide.**

ACTIVITY - Antidiabetic.

No test details for antidiabetic activity are given.

MECHANISM OF ACTION - None given.

USE - The pharmaceutical formulation comprising **crystalline nateglinide** form of A, C, D, F, G, I, J, K, M, N O, Q, T, V, Y, gamma, epsilon, theta or omega is useful to lower the blood sugar level (claimed).

ADVANTAGE - The new polymorphic forms of **nateglinide** provides a new opportunity to improve the performance characteristics of a pharmaceutical product.

Dwg.0/64

TECH UPTX: 20040310
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation (Claimed): Preparation of **nateglinide** form B comprises preparing a suspension of **nateglinide** in a 5-6C hydrocarbon, adding a solvent of an alcohol, ester and/or ketone to the suspension to obtain a solution, **crystallizing nateglinide** form B from the solution in the absence of stirring and recovering the **nateglinide** form B.

The **crystallization** is carried out by seeding and cooling at higher than 15 degrees C. Preparation of other **crystal** forms comprises heating one **crystal** form to obtain another or extracting the **crystal** form from a solvent.
Preferred Reagents: The hydrocarbon is heptane, hexane, toluene and xylene. The solvent is methanol, ethanol, isopropanol, n-butanol, n-propanol, acetone or ethyl acetate.

L3 ANSWER 4 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2004-108803 [11] WPIDS
CR 2004-180282 [17]; 2004-594140 [57]
DNC C2004-044538
TI Preparation of trans-4-isopropylcyclohexane acid chloride as intermediate in preparing **nateglinide** comprises reaction between thionyl chloride and acid chloride in the presence of organic amide.
DC B05
IN DOLITZKY, B; GOMEL, B; GOZLAN, Y; SHAPIOR, E; YAHALOMI, R; SHAPIRO, E
PA (TEVA-N) TEVA PHARM IND LTD; (TEVA-N) TEVA PHARM USA INC
CYC 105
PI WO 2004005240 A1 20040115 (200411)* EN 31
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
AU 2003253971 A1 20040209 (200450)
AU 2003256454 A1 20040123 (200459)
ADT WO 2004005240 A1 WO 2003-US21238 20030703; AU 2003253971 A1 AU 2003-253971 20030718; AU 2003256454 A1 AU 2003-256454 20030703
FDT AU 2003253971 A1 Based on WO 2004009532; AU 2003256454 A1 Based on WO 2004005240
PRAI US 2003-479016P 20030616; US 2002-393495P 20020703;
US 2002-396904P 20020718; US 2002-413622P 20020925;
US 2002-414199P 20020926; US 2002-423750P 20021105;
US 2002-432093P 20021210; US 2002-432962P 20021212;
US 2003-442109P 20030123; US 2003-449791P 20030224;
US 2003-614266 20030703
AB WO2004005240 A UPAB: 20040915
NOVELTY - Preparing trans-4-isopropylcyclohexane acid chloride comprises combining trans-4-isopropylcyclohexane carboxylic acid with thionyl chloride in the presence of a 1-6C organic amide to obtain trans-4-isopropylcyclohexane acid chloride free of its corresponding cis isomer; and recovering the trans-4-isopropylcyclohexane acid chloride.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a process for preparing **nateglinide** by combining trans-4-isopropylcyclohexane carboxylic acid with thionyl chloride in the presence of a 1-6C organic amide to obtain trans-4-isopropylcyclohexane acid chloride free of its corresponding cis isomer; converting the acid chloride to **nateglinide**; and recovering the **nateglinide**

.

ACTIVITY - Antidiabetic.

MECHANISM OF ACTION - None given.

USE - For preparing trans-4-isopropylcyclohexane acid chloride as an intermediate in preparing **nateglinide** for the treatment of type II diabetes.

ADVANTAGE - The cis-isomer is not formed nor detected in amounts of less than 0.05% even at elevated temperature (60-80 deg. C) in the reaction between thionyl chloride and trans-isopropylcyclohexane

carboxylic acid in the presence of an organic amide catalyst.
Dwg.0/3

TECH UPTX: 20040213

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Process: The combining is carried out by adding 0.05-10 wt.% amide to 1-5 acid equivalents of thionyl chloride at 10-60 degrees C. The reaction mixture is then maintained for 1-5 hours. The **nateglinide** may be prepared by combining a solution of a tri-alkyl amine salt of D-phenylalanine with trans-4-isopropylcyclohexane acid chloride in a 1-7C amide to form **nateglinide**; and recovering the **nateglinide.** The **nateglinide** may be prepared in a two-phase system by preparing an aqueous solution of an alkaline earth or alkali metal salt of D-phenylalanine; combining the aqueous solution with a water-immiscible organic solvent containing trans-4-isopropylcyclohexane acid chloride to form an aqueous and an organic phase, wherein **nateglinide** forms through reaction between the D-phenylalanine and the trans-4-isopropylcyclohexane acid chloride; and recovering the **nateglinide** . Preparing **nateglinide** Form Z comprises preparing an aqueous solution of an alkali metal or an alkali earth metal salt of **nateglinide**; acidifying the solution to precipitate **nateglinide**; and recovering the **nateglinide** Form Z. The aqueous solution contains water free of a co-solvent. Preparing **nateglinide** further comprises **crystallizing** /recrystallizing.

Preferred Composition: The weight ratio of the cis isomer to the trans isomer is less than 0.03%.

Preferred Compounds: The combining is carried out in a solvent, preferably aromatic or saturated hydrocarbon, ester or ether. The tri-alkyl amine is triethyl amine. The organic amide is N,N-dimethylacetamide, N-methylpyrrolidone or preferably N,N-dimethylformamide. The water-immiscible organic solvent is 5-12C hydrocarbon, preferably toluene, heptane or ethyl acetate.

L3 ANSWER 5 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2004-081844 [08] WPIDS
DNC C2004-033612
TI New **crystal** form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine useful for lowering blood glucose level.
DC A96 B05
IN SUTTON, P A
PA (NOVS) NOVARTIS AG; (NOVS) NOVARTIS PHARMA GMBH
CYC 90
PI WO 2003087038 A1 20031023 (200408)* EN 5
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE SI SK TR
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LT LU LV MA MD MK MN MX NI NO NZ OM PH PL PT RO RU SC SE SG SK TJ TM TN TR TT UA US UZ VC VN YU ZA ZW
AU 2003242520 A1 20031027 (200436)
ADT WO 2003087038 A1 WO 2003-EP3864 20030414; AU 2003242520 A1 AU 2003-242520 20030414
FDT AU 2003242520 A1 Based on WO 2003087038
PRAI US 2002-372625P 20020415
AB WO2003087038 A UPAB: 20040202
NOVELTY - A **crystal** form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (**nateglinide**) having melting point of 108 deg. C, or its solvate is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the production of R'-type **crystal** form of **nateglinide**

involving:
(a) dissolving **nateglinide** in any of its forms in a solvent (S1) in which **nateglinide** is readily soluble at an ambient temperature to form a solution;
(b) treating the solution with another solvent (S2) which is miscible with (S1) and in which **nateglinide** is poorly soluble to induce precipitation of R'-type **crystals** of **nateglinide**; and
(c) isolating and drying the precipitate **crystal** form of **nateglinide.**
ACTIVITY - Antidiabetic.
MECHANISM OF ACTION - None given.
USE - For lowering blood glucose level in human.
ADVANTAGE - The **nateglinide** in any of its form, such as hydrates, methanolates, ethanolates and acetonates can be used for the production of R'-type **crystal.**
Dwg.0/2

TECH UPTX: 20040202
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Method: The **crystal** form of **nateglinide** is induced by stirring, cooling or adding seed **crystals** of **nateglinide.** The ambient temperature is from room temperature to the boiling point of the solvent (preferably room temperature). The **crystal** form of **nateglinide** is dried under atmospheric or reduced pressure (preferably reduced pressure) at room temperature to 70 degrees Celsius (preferably room temperature to 50 degrees Celsius).
Preferred Components: (S1) is a mixture of ethanol (50 vol.%) and toluene. (S2) is water containing hydroxypropylmethylcellulose (1%). The ratio of (S1) and (S2) is 1:7 vol.

L3 ANSWER 6 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-853914 [79] WPIDS
DNC C2003-240851
TI New **crystalline nateglinide** forms A, M and P are antiglycemic agents and antidiabetic agents.
DC B05
IN KOGUCHI, Y; NAKAO, T; SUMIKAWA, M
PA (AJIN) AJINOMOTO CO INC
CYC 103
PI WO 2003087039 A1 20031023 (200379)* JA 17
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
AU 2003236243 A1 20031027 (200436)
ADT WO 2003087039 A1 WO 2003-JP4686 20030414; AU 2003236243 A1 AU 2003-236243 20030414
FDT AU 2003236243 A1 Based on WO 2003087039
PRAI JP 2002-111963 20020415
AB WO2003087039 A UPAB: 20031208
NOVELTY - **Crystalline nateglinide** forms A, M and P are new.
DETAILED DESCRIPTION - **Crystalline nateglinide** of formula (I) forms A, M and P are new.
USE - **Nateglinide** is an antiglycemic agent and antidiabetic agent.
ADVANTAGE - Have improve stability and solubility.
Dwg.0/3

TECH UPTX: 20031208
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred **Crystalline** Forms: **Crystalline** forms have the following powder X-ray diffraction peaks (2 theta) Form A 4.4, 5.2, 15.7 and 18.5 degrees; form M 6.0, 14.2, 15.2 and 18.8 degrees and form P 4.8, 5.3 14.3 and 15.2 degrees.
Preparation: Preparation of **crystalline** A form e.g. comprises:
(1) dissolving **nateglinide** in a solvent having high solubility for **nateglinide** and adding a solvent with poor solubility for **nateglinide** or dissolving **nateglinide** in a mixture of solvents having high and poor solubility for **nateglinide** (preferably ethanol and water);
(2) cooling the mixture (preferably to 10 degrees C) to precipitate **crystals**; and
(3) filtering and drying at 30-80 (preferably 40-60) degrees C.
Preparation of **crystalline** form A and P form comprises e.g. heating **crystalline** form B at 60 degrees C or more (preferably 80 degrees C or more). **Crystalline** form M is prepared e.g. by heating **crystalline** form B at 40-100 (preferably 50-70) degrees C and 60-95 (preferably 70-90)% relative humidity.

L3 ANSWER 7 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-748369 [70] WPIDS
DNC C2003-205231
TI New salt of **nateglinide** useful for treating, e.g. diabetes, cardiovascular or related diseases, e.g. hyperglycemia, hyperlipidaemia, obesity, diabetes retinopathy, diabetic neuropathy, glomerulosclerosis or stroke.
DC B05
IN DE LA CRUZ, M; PARKER, D J; SUTTON, P A; VIVILECCHIA, R V
PA (NOVS) NOVARTIS AG; (NOVS) NOVARTIS PHARMA GMBH
CYC 90
PI WO 2003076393 A1 20030918 (200370)* EN 23
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE SI SK TR
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LT LU LV MA MD MK MN MX NI NO NZ OM PH PL PT RO RU SC SE SG SK TJ TM TN TR TT UA US UZ VC VN YU ZA ZW
AU 2003214112 A1 20030922 (200431)
ADT WO 2003076393 A1 WO 2003-EP2447 20030310; AU 2003214112 A1 AU 2003-214112 20030310
FDT AU 2003214112 A1 Based on WO 2003076393
PRAI US 2002-363178P 20020311
AB WO2003076393 A UPAB: 20031030
NOVELTY - A salt of **nateglinide** (I) having a melting point of 50-300 deg. C is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) A composition comprising (I); and
(2) A method for the treatment of diabetes, cardiovascular disease or related conditions, comprising administration of (I).
ACTIVITY - Antidiabetic; Antilipemic; Anorectic; Ophthalmological; Neuroprotective; Nephrotropic; Vasotropic; Antiulcer; Antiinflammatory; Cardiant; Hypotensive; Antianginal; Cerebroprotective; Dermatological; Antiarthritic; Osteopathic; Vasotropic; Cardiovascular-Gen.
Test details are described, but no results given.
MECHANISM OF ACTION - None given.
USE - (I) is used for treating diabetes, cardiovascular or related diseases, e.g. hyperglycemia, hyperinsulinaemia, hyperlipidaemia, insulin resistance, impaired glucose metabolism, obesity, diabetes retinopathy,

macular degeneration, cataracts, diabetic neuropathy, glomerulosclerosis, erectile dysfunction, premenstrual syndrome, vascular restenosis, ulcerative colitis, coronary heart disease, hypertension, angina pectoris, myocardial infarction, stroke, skin and connective tissue disorder, foot ulcerations, metabolic acidosis, arthritis, osteoporosis, polycystic ovary syndrome or impaired glucose tolerance (all claimed).

ADVANTAGE - The salt of **nateglinide** has a higher degree of dissociation in water, increased biological availability of the salts, salt hydrates, or salt anions in the case of solid dosage forms. For different relative humidities at room temperature, the salts shows (with the exception of potassium and a calcium salt) practically no water absorption or water loss over a wide range of humidities and for periods of few hours, e.g. four hours. The melting point of the salts will not be changed by storing under different relative humidities, except for the melting point of those salts that are hygroscopic or moderately hygroscopic. (I) has a water solubility of at least 0.18 (preferably at least 0.4, especially 40) mg/ml.

Dwg.0/0

TECH UPTX: 20031030

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Compound: (I) is confirmed by X-ray powder diffraction (XRPD) pattern and is present in an amorphous and/or **crystalline** form.

The ratio of **nateglinide** anion to cation is 1:1 or 2:1.

The salt loses 0.1-14 (preferably 0.1-0.9)% of its mass on heating.

(I) has a bulk density of 0.1-0.6 g/cm3.

Preferred Cation: In (I), the cation is a sodium ion (Na+), potassium ion (K+), calcium ion (Ca2+), magnesium ion (Mg2+) or the protonated form of tris(hydroxymethyl)-aminomethane or N-methyl-D-glucamine or lysine.

Preferred Composition: The composition also comprises at least one of vitamins, nutrition supplements, active substances, **nateglinide** or repaglinide.

The active substance is an insulin sensitizer, insulin secretion enhancer, dipeptidyl peptidase IV inhibitor, ACE inhibitor or angiotensin II inhibitor.

L3 ANSWER 8 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-111806 [10] WPIDS
DNC C2003-028518
TI New **crystalline** complex between either (D) or (L) enantiomers of natural amino acids and amorphous C-aryl glucoside compounds useful for treating e.g. diabetes.
DC B03
IN GOUGOUTAS, J Z
PA (GOUG-I) GOUGOUTAS J Z; (BRIM) BRISTOL-MYERS SQUIBB CO
CYC 101
PI WO 2002083066 A2 20021024 (200310)* EN 80
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2003064935 A1 20030403 (200325)
EP 1385856 A2 20040204 (200410) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
AU 2002254567 A1 20021028 (200433)
US 6774112 B2 20040810 (200453)
ADT WO 2002083066 A2 WO 2002-US11066 20020408; US 2003064935 A1 Provisional US

2001-283097P 20010411, US 2002-117914 20020408; EP 1385856 A2 EP 2002-723801 20020408, WO 2002-US11066 20020408; AU 2002254567 A1 AU 2002-254567 20020408; US 6774112 B2 Provisional US 2001-283097P 20010411, US 2002-117914 20020408

FDT EP 1385856 A2 Based on WO 2002083066; AU 2002254567 A1 Based on WO 2002083066

PRAI US 2001-283097P 20010411; US 2002-117914 20020408

AB WO 200283066 A UPAB: 20030211

NOVELTY - A **crystalline** complex between either (D) or (L) enantiomers of natural amino acid and amorphous C-aryl glucoside compound is new.

DETAILED DESCRIPTION - **Crystalline** complexes between either (D) or (L) enantiomers of natural amino acids and compound of formula (I) are new.

R1, R2 and R2a = H, OH, OR5, alkyl, -OCHF2, -OCF3, -SR5a or halo;

R3 and R4 = H, OH, OR5b, (cyclo)alkyl, CF3, -OCHF2, -OCF3, halogen, -CONR6R6a, -CO2R5c, -CO2H, -COR6b, -CH(OH)R6c, -CH(OR5d)R6d, -CN, -NHCOR5e, -NHSO2R5f, -NHSO2Aryl, -SR5g, -SOR5h, SO2R5i or 5 - 7-membered heterocycle (containing 1 - 4 heteroatoms of N, O, S, SO and/or SO2);

R3+R4 and NR6+R6a = annelated 5 - 7-membered carbocycle or heterocycle (both containing 1 - 4 heteroatoms of N, O, S, SO and/or SO2));

R5 and R5a - R5i = alkyl;

R6 and R6a - R6d = H, alkyl, (alkyl)aryl or cycloalkyl.

INDEPENDENT CLAIMS are included for the following:

(1) A pharmaceutical combination (A1) comprising complex of either the (D) or (L) enantiomer of natural amino acids with (I) and a component (G1) selected from an antidiabetic agent (G) other than an SGLT2 inhibitor, an agent for treating the complications of diabetes, an anti-obesity agent, an antihypertensive agent, an antiplatelet agent, an antiatherosclerotic agent and/or a lipid-lowering agent (preferably G); and

(2) Treating type II diabetes involving administering the complex of (I) alone or in combination with another antidiabetic agent, an agent for treating the complications of diabetes, an anti-obesity agent, an antihypertensive agent, an antiplatelet agent, an antiatherosclerotic agent and/or a hypolipidemic agent.

ACTIVITY - Antidiabetic; Ophthalmological; Neuroprotective; Vulnerary; Anorectic; Antiarteriosclerotic; Hypotensive; Nephrotropic.

MECHANISM OF ACTION - Inhibitors of sodium dependent glucose transporters.

USE - Compound (I) is used for treating or delaying the progression or onset of diabetes, diabetic retinopathy, diabetic neuropathy, diabetic nephropathy, delayed wound healing, insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, hyperlipidemia, obesity, hypertriglyceridemia, Syndrome X, diabetic complications, atherosclerosis or hypertension or for increasing high density lipoprotein levels and for treating type II diabetes (claimed).

ADVANTAGE - The complex normalizes the plasma glucose by enhancing the excretion of glucose in the urine, thus improves insulin sensitivity and delays the development of diabetic complications.

Dwg.0/0

TECH UPTX: 20030211

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: The complex is prepared by:

(1) Dissolving (I) in a water miscible solvent that is heated to 50 - 80 degrees C;

(2) Transferring the solution rapidly to a 50 - 80 degrees C aqueous or alcoholic solution containing either one or two equivalents of either the (D) or (L) enantiomer of a natural amino acid; and

(3) Upon slowly cooling, isolating the **crystals** of the desired complex form by filtration.
Preferred Compound: The compound is a compound of formula (Ia).
R'1 = H, alkoxy, halogen or lower alkyl;
R'4 = lower alkyl, R5aO, -OCHF2, SR5e, S(O)R5e or S(O)2R5e.
Preferred Complex: The complex comprises L-phenylalanine:1-(-(3-(4-difluoromethoxybenzyl)-4-methylphenyl)-beta-D-glucopyranoside in a ratio of 1:1, L-Phenylalanine:1-(-(3-(4-methylthiobenzyl)-4-methylphenyl)-beta-D-glucopyranoside in a ratio 1:1, L-phenylalanine:1-(-(3-(4-ethylbenzyl)-phenyl)-beta-D-glucopyranoside in a ratio of 1:1, L-phenylalanine:1-(-(3-(4-ethylbenzyl)-phenyl)-beta-D-glucopyranoside in a ratio of 2:1, L-proline:1-(-(3-(4-ethylbenzyl)-phenyl)-beta-D-glucopyranoside in a ratio of 2:1, L-proline:1-(-(3-(4-ethylbenzyl)-phenyl)-beta-D-glucopyranoside in a ratio of 1:1, L-proline:1-(-(3-(4-methylthiobenzyl)-4-methylphenyl)-beta-D-glucopyranoside in a ratio of 1:1 or D-phenylalanine:1-(-(3-(4-methylthiobenzyl)-4-methylphenyl)-beta-D-glucopyranoside in a ratio of 1:1.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Combination: A weight ratio of the complex of either the (D) or (L) enantiomer to (G) or to the lipid-lowering agent is 0.01 - 300:1.
Preferred Components: (G) is at least one of a biguanide, a sulfonyl urea, a glucosidase inhibitor, a PPAR gamma agonist, a PPAR alpha/gamma dual agonist, an aP2 inhibitor, a DP4 inhibitor, n insulin sensitizer, a glucagons-like peptide-1 (GLP-1), insulin, a meglitinide, a PTP1B inhibitor, a glycogen phosphorylase inhibitor and/or a glucose-6-phosphatase inhibitor, preferably at least one of metformin, glyburide, glimepride, glipyride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, G1-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, **nateglinide**, KAD1129, AR-HO39242, GW-409544, KRP297, AC2993, LY315902 and/or NVP-DPPD-728A. The anti-obesity agent is a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin and dopamine reuptake inhibitor, a thyroid receptor beta compound and/or an anorectic agent (preferably orlistat, ATL-962, AJ9677, L750355, CP331648, sibutramine, topiramate, axokine, dexamphetamine, phentermine, phenylpropanolamine and/or mazindol). The lipid lowering agent is an MTP inhibitor, an HMG CoA reductase inhibitor, a squalane synthetase inhibitor, a fibric acid derivative, an upregulator of LDL receptor activity, a lipoxygenase inhibitor or an ACAT inhibitor (preferably pravastatin, lovastatin, simvastatin, atorvastatin, cerivastatin, fluvastatin, nisvastatin, visastatin, atavastatin, rosuvastatin, fenofibrate, gemfibrozil, clofibrate, avasimbe, TS-962, MD-700 and/or LY295427).

L3 ANSWER 9 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-713487 [77] WPIDS
DNC C2002-202321
TI Combination used for treating e.g. hypertension, obesity, diabetic neuropathy and arthritis comprises **nateglinide** or repaglinide and additional antidiabetic compound e.g. insulin.
DC B02 B05
IN VILLHAUER, E B
PA (NOVS) NOVARTIS AG; (NOVS) NOVARTIS PHARMA GMBH; (VILL-I) VILLHAUER E B; (NOVS) NOVARTIS-ERFINDUNGEN VERW GES MBH
CYC 88
PI WO 2002072146 A2 20020919 (200277)* EN 30
RW: AT BE CH CY DE DK EA ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH HR HU ID IL IN IS JP KE KG KP KR KZ

LC LK LT LU LV MA MD MK MN MX NO NZ OM PH PL PT RO RU SE SG SI SK TJ TM TN TR TT UA US UZ VN YU ZA ZW

EP 1385549 A2 20040204 (200410) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

AU 2002254940 A1 20020924 (200433)

US 2004143015 A1 20040722 (200449)

ADT WO 2002072146 A2 WO 2002-EP2665 20020311; EP 1385549 A2 EP 2002-724221 20020311, WO 2002-EP2665 20020311; AU 2002254940 A1 AU 2002-254940 20020311; US 2004143015 A1 WO 2002-EP2665 20020311, US 2003-471253 20030910

FDT EP 1385549 A2 Based on WO 2002072146; AU 2002254940 A1 Based on WO 2002072146

PRAI US 2001-275098P 20010312; US 2003-471253 20030910

AB WO 200272146 A UPAB: 20021129

NOVELTY - Combination comprises **nateglinide** or repaglinide, at least one additional antidiabetic compound and optionally at least one carrier.

DETAILED DESCRIPTION - Combination comprises **nateglinide** or repaglinide, at least one additional antidiabetic compound and optionally at least one carrier. The antidiabetic compound comprises insulin signaling pathway modulator, compounds influencing a dys-regulated hepatic glucose production, pyruvate dehydrogenase kinase (PDHK) inhibitor, inhibitors of gastric emptying, insulin, inhibitors of glycogen synthase kinase-3, retinoid X receptor (RXR) agonists, agonists of human beta -3 adrenergic receptor, agonists of uncoupling proteins (UCPs), non-glitazone type PPAR- gamma , dual PPAR- gamma /PPAAR- alpha agonists, antidiabetic vanadium containing compounds, incretin hormones, beta -cell imidazoline receptor antagonist, miglitol or alpha 2-adrenergic antagonists.

The active ingredients are contained in the free form or in the form of their salts.

An INDEPENDENT CLAIM is also included for a commercial package comprising the combination together with instructions for simultaneous, separate or sequential used in the prevention, delay of progression or treatment of metabolic disorders or for improving the bodily appearance.

ACTIVITY - Antidiabetic; Ophthalmological; Anorectic; Nephrotropic; Vasotropic; Gynecological; Antiinflammatory; Antiulcer; Cardiant; Hypotensive; Cerebroprotective; Dermatological; Antiarthritic; Osteopathic.

MECHANISM OF ACTION - Iinsulin signaling pathway modulator; Pyruvate dehydrogenase kinase inhibitor; Retinoid X receptor agonist; Glycogen synthase kinase-3 inhibitor; Human beta -3 adrenergic receptor; Uncoupling protein agonist; beta -cell imidazoline receptor antagonist; Miglitol antagonist; alpha 2-adrenergic antagonist; Non-glitazone type PPAR- gamma , dual PPAR- gamma /PPAAR- alpha agonist.

No biological tests or results are given in the source material.

USE - Used for the prevention, delay of progression or treatment of metabolic disorders and for cosmetic treatment to obtain body weight loss (all claimed). The combination is used for treating hyperglycemia, hyperinsulinaemia, hyperlipidaemia, insulin resistance, impaired glucose metabolism, obesity, diabetic retinopathy, macular degeneration, cataracts, diabetic nephropathy, glomerulosclerosis, diabetic neuropathy, erectile dysfunction, premenstrual syndrome, vascular restenosis, ulcerative colitis, coronary heart disease, hypertension, angina pectoris, myocardial infarction, stroke, skin and connective tissue disorders, foot ulceration, metabolic acidosis, arthritis, osteoporosis and impaired glucose tolerance.

ADVANTAGE - The combination results in a beneficial, especially a synergistic, therapeutic effect. The combination also provides efficacy, a broader variety of therapeutic treatment and beneficial effects on

diseases and conditions associated with diabetes, which includes less gain of weight, compared to a mono-therapy applying only one of the active ingredients of the combination.
Dwg.0/0

TECH UPTX: 20021129
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compounds: The combination comprises 3-(4-(2-(2,3-dihydrobenzo(1,4)thiazin-4-yl)-ethoxy)-phenyl)-2-ethoxy propionic acid as a dual PPAR-gamma/PPAR-alpha agonist. The combination also includes at least one active compound comprising glitazone, sulfonylurea derivative, metformin, acarbose and/or their salts. The combination is in the form of a combined preparation or a pharmaceutical composition. The neteglinide is present in the B-type or H-type **crystal** modification.

L3 ANSWER 10 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-507933 [54] WPIDS
DNC C2002-144389
TI Process for producing **nateglinide crystals** useful for treating diabetes involves reacting trans-4-isopropylcyclohexylcarbonyl chloride with D-phenylalanine in ketone and water in presence of alkali.
DC B05
IN NISHI, S; TAKAHASHI, D; TAKAHASHI, S
PA (AJIN) AJINOMOTO CO INC; (AJIN) AJINOMOTO KK
CYC 98
PI WO 2002032854 A1 20020425 (200254)* JA 15
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001094265 A 20020429 (200255)
EP 1334963 A1 20030813 (200355) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
BR 2001014729 A 20031014 (200374)
KR 2003059203 A 20030707 (200377)
US 2004030182 A1 20040212 (200412)
JP 2002536038 X 20040226 (200416)
MX 2003003484 A1 20030701 (200423)
CN 1481356 A 20040310 (200437)
ADT WO 2002032854 A1 WO 2001-JP9069 20011016; AU 2001094265 A AU 2001-94265 20011016; EP 1334963 A1 EP 2001-974875 20011016, WO 2001-JP9069 20011016; BR 2001014729 A BR 2001-14729 20011016, WO 2001-JP9069 20011016; KR 2003059203 A KR 2003-705388 20030417; US 2004030182 A1 Cont of WO 2001-JP9069 20011016, US 2003-418105 20030418; JP 2002536038 X WO 2001-JP9069 20011016, JP 2002-536038 20011016; MX 2003003484 A1 WO 2001-JP9069 20011016, MX 2003-3484 20030416; CN 1481356 A CN 2001-820658 20011016
FDT AU 2001094265 A Based on WO 2002032854; EP 1334963 A1 Based on WO 2002032854; BR 2001014729 A Based on WO 2002032854; JP 2002536038 X Based on WO 2002032854; MX 2003003484 A1 Based on WO 2002032854
PRAI JP 2000-317604 20001018
AB WO 200232854 A UPAB: 20020823
NOVELTY - A process for producing **nateglinide crystals** involves:
(i) reacting trans-4-isopropylcyclohexylcarabonyl chloride with D-phenylalanine in a mixed solvent, consisting of a ketone and water in the presence of an alkali; and
(ii) adding an acid to the resulting reaction mixture and subjected

to **crystallization** while regulating the temperature and the ketone solvent concentration.

DETAILED DESCRIPTION - A process for producing **nateglinide crystals** involves:

(i) reacting trans-4-isopropylcyclohexylcarbonyl chloride with D-phenylalanine in a mixed solvent, consisting of a ketone and water in the presence of an alkali; and

(ii) adding an acid, providing an acidic condition to the resulting reaction mixture, containing **nateglinide** and subjected to **crystallization** while regulating the temperature (between 58 - 72 deg. C) and the ketone solvent concentration (between 9 to up to but not including 22 wt%).

USE - For producing **nateglinide crystals**, which can be used as an oral medicine for treating diabetes.

ADVANTAGE - The process is efficient even on an industrial production scale.

Dwg.0/0

TECH UPTX: 20020823

TECHNOLOGY FOCUS - CHEMICAL ENGINEERING - Preferred Process: The adjustment of the ketone solvent concentration is conducted by adding a ketone (preferably acetone) to the reaction mixture, which is an acylation reaction solution. The ketone is at a concentration of 12 - 16 wt% in the reaction system.

Preferred **Crystal**: The **crystal** of the **nateglinide** is a H-type **crystal** having a mean long diameter of 1 mm or more and a mean short diameter of 0.1 mm or more.

L3 ANSWER 11 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-500188 [53] WPIDS
DNC C2002-141632
TI Hydrophilic drug preparation comprises **nateglinide** B **crystals** and has contact angle to water surface of 111 degrees or less useful as an hypoglycemic agent.
DC A96 B05
IN MAKINO, C; NINOMIYA, N; YABUKI, A
PA (AJIN) AJINOMOTO CO INC; (AJIN) AJINOMOTO KK
CYC 98
PI WO 2002040010 A1 20020523 (200253)* JA 26
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001096000 A 20020527 (200261)
EP 1334721 A1 20030813 (200355) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
KR 2003042028 A 20030527 (200361)
BR 2001014897 A 20030812 (200367)
US 2004029968 A1 20040212 (200412)
JP 2002542384 X 20040603 (200436)
CN 1482904 A 20040317 (200437)
ADT WO 2002040010 A1 WO 2001-JP9292 20011023; AU 2001096000 A AU 2001-96000 20011023; EP 1334721 A1 EP 2001-976818 20011023, WO 2001-JP9292 20011023; KR 2003042028 A KR 2003-705635 20030423; BR 2001014897 A BR 2001-14897 20011023, WO 2001-JP9292 20011023; US 2004029968 A1 Cont of WO 2001-JP9292 20011023, US 2003-420886 20030423; JP 2002542384 X WO 2001-JP9292 20011023, JP 2002-542384 20011023; CN 1482904 A CN 2001-821218 20011023
FDT AU 2001096000 A Based on WO 2002040010; EP 1334721 A1 Based on WO

2002040010; BR 2001014897 A Based on WO 2002040010; JP 2002542384 X Based on WO 2002040010

PRAI JP 2000-324374 20001024

AB WO 200240010 A UPAB: 20020820

NOVELTY - Hydrophilic drug preparation comprises **nateglinide** B **crystals** and has a contact angle to the surface of water of 111 deg. or less.

ACTIVITY - Antidiabetic.

MECHANISM OF ACTION - None given.

USE - As a hydrophillic drug preparation for administering **nateglinide** B **crystals** useful as an hypoglycemic agent.

ADVANTAGE - Have quick release with high elution properties and are easily produced.

Dwg.0/0

TECH UPTX: 20020820

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: Preparation is film or sugar coated, has a contact angle to the surface of water of 100 (preferably 90) degrees or less and contains a hydrophilic substance (preferably a hydrophillic polymer, surfactant, sugar, sugar alcohol or salt)

L3 ANSWER 12 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2002-462521 [49] WPIDS

CR 1999-204733 [17]; 2000-170837 [15]; 2001-432562 [46]; 2001-522427 [57]; 2001-595790 [67]; 2002-082346 [11]; 2002-215543 [27]; 2002-215909 [27]; 2002-315576 [35]; 2002-328338 [36]; 2002-635742 [68]; 2002-666828 [71]; 2002-696871 [75]; 2003-015683 [01]; 2003-198106 [19]; 2003-238931 [23]; 2003-417948 [39]; 2003-627162 [59]; 2003-776923 [73]

DNN N2002-364678 DNC C2002-131331

TI Administering and distributing substance, e.g. pharmaceutically active agent, to target through bloodstream of organism by monitoring blood flow parameter(s), and adjusting distribution parameter.

DC A96 B05 B07 P31 S03 S05

IN KENSEY, K

PA (KENS-I) KENSEY K; (RHEO-N) RHEOLOGICS INC

CYC 97

PI US 2002032149 A1 20020314 (200249)* 46

WO 2002079778 A2 20021010 (200277) EN

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2002306461 A1 20021015 (200432)

ADT US 2002032149 A1 CIP of US 1997-919906 19970828, CIP of US 1999-439795 19991112, CIP of US 2000-501856 20000210, CIP of US 2000-628401 20000801, CIP of US 2000-727950 20001201, CIP of US 2001-819924 20010328, US 2001-841389 20010424; WO 2002079778 A2 WO 2002-US3984 20020207; AU 2002306461 A1 AU 2002-306461 20020207

FDT US 2002032149 A1 CIP of US 6019735, CIP of US 6322524, CIP of US 6322525; AU 2002306461 A1 Based on WO 2002079778

PRAI US 2001-841389 20010424; US 1997-919906 19970828;
US 1999-439795 19991112; US 2000-501856 20000210;
US 2000-628401 20000801; US 2000-727950 20001201;
US 2001-819924 20010328; US 2001-828761 20010409;
US 2001-839785 20010420

AB US2002032149 A UPAB: 20040520

NOVELTY - A substance (I) is administered and distributed (to a target) through a bloodstream of an organism by monitoring a blood flow

parameter(s) of the bloodstream, after which a distribution parameter is adjusted by altering the parameter(s).

DETAILED DESCRIPTION - A substance (I) is administered and distributed (to a target) through a bloodstream of an organism by monitoring a blood flow parameter(s) of the bloodstream, after which a distribution parameter is adjusted by altering the parameter(s). The parameter is circulating blood, absolute, effective, low shear or high shear viscosities, shear rate of circulating blood, work of heart, contractility of heart, thrombogenicity, platelet aggregation, lubricity, red blood cell deformability, thixotropy, yield stress, coagulability, coagulation time, agglutination, clot retraction, clot lysis time, sedimentation rate, or prothrombin rate.

USE - The method is used for distributing and administering a substance, e.g. pharmaceutically active agent, through a bloodstream of an organism such as a human. It is used for utilizing the viscosity of the circulating blood of a living being, for diagnostics and treatment.

ADVANTAGE - The method provides data in a short span of time, with minimal invasiveness, and without the need to directly measure pressure, flow, and volume.

Dwg.0/22

TECH UPTX: 20020802

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Components: The target is a cell, tissue or a system.

The blood flow parameter is selected from intravenous diluents, red blood cell deformability agents, antiurea agents, oral contraceptives, anti-diabetic agents, antiarrythmics, antihypertensives, antihyperlipidemics, antiplatelet agents, anti-coagulants, appetite suppressants, antiobesity agents, blood modifiers, smoking deterrent agents, nutritional supplements, cholesterol-lowering agents, triglyceride-lowering agents, lubricants, homocysteine-reducing agents, vitamin supplements, beta-blockers, calcium channel blockers, ACE inhibitors, ACE-II inhibitors, vasodilators, blood pressure reducing agents, viscosity reducing agents, contractility reducing agents, hemodilution agents, adhesiveness minimizing agents, peripheral antiadrenergic/sympatholytics, anti-thrombogenic agent, warfarin, heparin, surfactants, saponifying agents, sodium bentonite magma, colloidal clays, colloidal silicon dioxide, micro-**crystalline** cellulose, gels of colloidal clays such as sodium bentonite, gels of organic polymers such as gelatin, agar, pectin, methylcellulose, or high-molecular-weight polyethylene glycol.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Component: (I) (1 - 100 wt.%) is a pharmaceutically active agent selected from levonorgestrel, estrogen, progestin, (ethinyl) estradiol, ethynodiol, medroxyprogesterone, desogestrel, cyproterone, norethindrone, gestodene, norgestrel, mestranol, norgestimate, metformin, acarbose, insulin, chlorpropamide, glipizide, glyburide, tolazamide, glimepiride, troglitazone, pioglitazone, repaglinide, losartan potassium, candesartan cilexetil, irbesartan, mitiglinide, trendolapril/verapamil, **nateglinide**, nifedipine, nisoldipine, nicardipine, bepridil, isradipine, nimodipine, felodipine, amlodipine, diltiazem, verapamil, isosorbide, mononitrate, isosorbide dinitrate, nitroglycerin, hydralazine, minoxidil, hydrochlorothiazide, chlorothiazide, indapamide, metolazone, furosemide, bumetanide, ethacrynic acid, torsemide, spironolactone, triamterene, acetazolamide, mannitol, atenolol, bisoprolol, pindolol, metoprolol, timolol, nadolol, propanolol, carvedilol, captopril, fosinopril, benazepril, lisinopril, perindopril, enalapril, quinapril, losartan, valsartan, eprosartan, trandorapril, fenoldopam, ramipril, doxazosin, milrinone, benidipine, lemakalim, fantofarone, lemildipine, pirmenol, clentiazem, nebivolol, oxodipine, sematilide, pranidipine, nifekalant, aranidipine, barnidipine, lacidipine, bucindolol, azelnidipine, dofetilide, ibutilide, watanidipine,

lercanidipine, landiolol, telmisartan, furnidipine, azimilide, CHF 1521, valsartan/hydrochlorothlazide, enalapril/nitrondipine, sotalol, arbutamine, olmesartan, conivaptan, sumatriptan, milrinone, lovastatin, atorvastatin, cerivastatin, simvastatin, fluvastatin, cholestyramine, colestipol, clofibrate, gemfibrosil, fenofibrate, pamaqueside, pitavastatin, phentermine, phendimetrazine, sibutramine, orlistat, aspirin, warfarin, enoxaparin, heparin, low molecular weight heparin, cilostazol, clopidogrel, ticlopidine, tirofiban, abciximab, dipyridamole, plasma protein fraction, human albumin, low molecular weight dextran, hetastarch, reteplase, alteplase, streptokinase, urokinase, dalteparin, filgrastin, immunoglogulin, ginkolide B, hirudins, foropafant, rocepafant, bivalirudin, dermatan sulfate mediolanum, eptilibatide, thrombomodulin, low molecular weight dermatan sulfate-opocrin, eptacog alfa, argatroban, fondaparinux sodium, tifacogin, lepirudin, desirudin, OP2000, melagatran, roxifiban, parnaparin sodium, human hemoglobin (Hemosol), bovine hemoglobin (Biopure), human hemoglobin (Northfield), antithrombin III, RSR 13, heparin-oral (Emisphere) transgenic antithrombin III, H37695, mesoglycan, CTC111, nicotine, buprorion, fasudil, ziconotide, amino acid preparations, minerals, electrolytes, vitamins, calcitriol, terbinafine, ticarcillin disodium, cefixime, meropenem, cefprozil, levofloxacin, cefpodoxime proxetil, imipenem, cefuroxime axetil, trovafloxacin, mupirocin, stavudine, didanosine, nevirapine, lamivudine, zidovudine, valcyclovir, ganciclovir, nefiracetam, remifentanil, sevoflurane, tiagabine, topiramate, lamotrigine, naratriptan, bromocriptine, tolcapone, oxaprozin, diclofenac, misoprostol, nabumetone, granisetron, dotarizine, RSR13, zonisamide, BMS204352, oxcarbazepine, tropisetron, irinotecan, topetecan, anastrozole, nilutamide, cladribine, gemcitabine, letrozole, vinorelbine, epirubicin, raloxifene, calcitonin, somatotropin, recombinant somatotropin, tolterodine, temiverine, meluadrine tartrate, lansoprazole, ropivacaine, bambuterol, israpafant, rupatadine, levosalbutamol, ARC68397AA, salbutamol (powder), salbutamol (inhalation), salbutamol (oral), salbutamol (powder inhalation), formoterol, salmeterol/fluticasone propionate, salmeterol MDI dose counter, salmeterol (inhalation), salmeterol hydrofluoroalkane, budesonide/formoterol, olopatadine, levobetaxolol, levobunolol, latanoprost/timolol, ketotifen, desferoxamine, leukine, sargramostin, or GM-CSF.

L3 ANSWER 13 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-372354 [40] WPIDS
DNC C2002-105446
TI Production of **nateglinide** B-form **crystals** containing no H-form **crystals**, by drying wet **crystals** of **nateglinide** solvate at low temperature until solvent disappears and performing **crystal** transformation.
DC B05
IN MARUO, M; MATSUZAWA, Y; MIYAZAKI, K; NISHINA, S; SUMIKAWA, M
PA (AJIN) AJINOMOTO CO INC; (AJIN) AJINOMOTO KK
CYC 98
PI WO 2002034713 A1 20020502 (200240)* JA 9
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001096001 A 20020506 (200257)
EP 1334964 A1 20030813 (200355) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
KR 2003059212 A 20030707 (200377)

US 2003229249 A1 20031211 (200382)
BR 2001014846 A 20040225 (200416)
JP 2002537707 X 20040304 (200417)
MX 2003003575 A1 20030701 (200423)
CN 1483018 A 20040317 (200437)

ADT WO 2002034713 A1 WO 2001-JP9293 20011023; AU 2001096001 A AU 2001-96001 20011023; EP 1334964 A1 EP 2001-976819 20011023, WO 2001-JP9293 20011023; KR 2003059212 A KR 2003-705671 20030424; US 2003229249 A1 Cont of WO 2001-JP9293 20011023, US 2003-421888 20030424; BR 2001014846 A BR 2001-14846 20011023, WO 2001-JP9293 20011023; JP 2002537707 X WO 2001-JP9293 20011023, JP 2002-537707 20011023; MX 2003003575 A1 WO 2001-JP9293 20011023, MX 2003-3575 20030423; CN 1483018 A CN 2001-821299 20011023

FDT AU 2001096001 A Based on WO 2002034713; EP 1334964 A1 Based on WO 2002034713; BR 2001014846 A Based on WO 2002034713; JP 2002537707 X Based on WO 2002034713; MX 2003003575 A1 Based on WO 2002034713

PRAI JP 2000-324375 20001024

AB WO 200234713 A UPAB: 20020626
NOVELTY - Production of **nateglinide** (N-(trans-4-isopropyl-cyclohexane carbonyl)-D-phenylalanine) B-form **crystals** containing no H-form **crystals**, comprises drying wet **crystals** of **nateglinide** solvate at a low temperature until the solvent disappears and performing **crystal** transformation.
ACTIVITY - Antidiabetic.
MECHANISM OF ACTION - None given.
USE - The **nateglinide** B-form **crystals** containing no H-form **crystals** are used as diabetes medicines.
ADVANTAGE - The **nateglinide** B-form **crystals** containing no H-form **crystals** can be produced on an industrial scale at low cost.
Dwg.0/0

TECH UPTX: 20020626
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Method: No H-form **crystals** are detected by DSC. **Crystallization** is performed at at most50degreesC. The **crystal** transformation is performed by heating to 60-110degreesC. Both processes of the low temperature drying and the **crystal** transformation are processes which are performed on an industrial scale.

L3 ANSWER 14 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-372336 [40] WPIDS
DNC C2002-105445
TI New composition comprises **nateglinide** in the amorphous state, useful for treatibg diabetes.
DC B05
IN MAKINO, C; NINOMIYA, N; YABUKI, A
PA (AJIN) AJINOMOTO CO INC; (AJIN) AJINOMOTO KK
CYC 98
PI WO 2002034254 A1 20020502 (200240)* JA 29
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001095999 A 20020506 (200257)
EP 1334720 A1 20030813 (200355) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

KR 2003042027 A 20030527 (200361)
BR 2001014896 A 20030812 (200367)
US 2004014815 A1 20040122 (200407)
CN 1482903 A 20040317 (200437)
JP 2002537308 X 20040826 (200456)

ADT WO 2002034254 A1 WO 2001-JP9291 20011023; AU 2001095999 A AU 2001-95999 20011023; EP 1334720 A1 EP 2001-976817 20011023, WO 2001-JP9291 20011023; KR 2003042027 A KR 2003-705634 20030423; BR 2001014896 A BR 2001-14896 20011023, WO 2001-JP9291 20011023; US 2004014815 A1 Cont of WO 2001-JP9291 20011023, US 2003-421898 20030424; CN 1482903 A CN 2001-821217 20011023; JP 2002537308 X WO 2001-JP9291 20011023, JP 2002-537308 20011023

FDT AU 2001095999 A Based on WO 2002034254; EP 1334720 A1 Based on WO 2002034254; BR 2001014896 A Based on WO 2002034254; JP 2002537308 X Based on WO 2002034254

PRAI JP 2000-324373 20001024

AB WO 200234254 A UPAB: 20020626

NOVELTY - Composition comprising **nateglinide** in the amorphous state, is new.

ACTIVITY - Antidiabetic. In oral bioavailability studies in beagles amorphous **nateglinide** had an AUC (mu g/ml.hr) of 22.29, a Cmax (mu g/ml) of 9.46 and a Tmax (hr) of 0.38. The corresponding values for **nateglinide crystalline** form H were 20.53, 8.93 and 0.38 respectively.

MECHANISM OF ACTION - None given.

USE - As preparations for administering **nateglinide** useful as an antidiabetic agent.

ADVANTAGE - Have rapid release properties.

Dwg.0/9

TECH UPTX: 20020626

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Composition: The composition comprises amorphous **nateglinide** prepared by removing the solvent (preferably aqueous ethanol) from a solution of **nateglinide** and a hydrophiliic compound (preferably a water soluble polymer, water swellable polymer, sugar alcohol or salt, especially methylcellulose SM-4, hydroxypropylcellulose SL, hydroxypropylcellulose SSL, polyethylene glycol, sorbitol, xylitol, mannitol or crospovidone).

L3 ANSWER 15 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-290407 [30] WPIDS
CR 2003-401332 [38]
DNC C2001-088908
TI Use of a combination of **nateglinide** with another antidiabetic compound for treating a metabolic disorder, e.g. diabetes and associated conditions, or for effecting weight loss.
DC A96 B05
IN ALLISON, M; GATLIN, M R; GUITARD, C; KARNACHI, A A; MANNION, R O; PONGOWSKI, M; BALL, M; KAMACHI, A A; BALL, M A
PA (NOVS) NOVARTIS AG; (NOVS) NOVARTIS-ERFINDUNGEN VERW GES MBH; (ALLI-I) ALLISON M; (BALL-I) BALL M A; (GATL-I) GATLIN M R; (GUIT-I) GUITARD C; (KARN-I) KARNACHI A A; (MANN-I) MANNION R O
CYC 95
PI WO 2001021159 A2 20010329 (200130)* EN 60
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
FR 2798592 A1 20010323 (200130)

FI 2001000683 A 20010515 (200140)
AU 2000079044 A 20010424 (200141)
CZ 2001001723 A3 20010815 (200157)
MX 2001004255 A1 20010801 (200238)
EP 1212077 A2 20020612 (200239) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
NO 2002001197 A 20020516 (200240)
BR 2000014525 A 20020611 (200248)
SK 2002000360 A3 20020702 (200253)
BE 1013726 A5 20020702 (200257)
KR 2002038758 A 20020523 (200274)
JP 2003509457 W 20030311 (200319) 83
US 2003162816 A1 20030828 (200357)
NZ 517280 A 20040227 (200418)
ZA 2002002107 A 20040331 (200426) 86
HU 2004000932 A2 20040728 (200454)

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PRAI GB 2000-21055 20000826; US 1999-398364 19990917; US 2000-545480 20000407

AB WO 200121159 A UPAB: 20040823

NOVELTY - **Nateglinide** (I), optionally in combination with another antidiabetic compound, can be used in the treatment of diabetes and associated conditions. The combination can also be used for effecting weight loss.

DETAILED DESCRIPTION - Use of a combination of **nateglinide** (I) and at least 1 other antidiabetic compound, selected from thiazolidine derivatives (glitazones), sulfonyl urea derivatives and metformin, present in the free form or as salts, for prevention, delay of progression or treatment of metabolic disorders, or for cosmetic treatment to effect a loss of body weight, is new.

INDEPENDENT CLAIMS are included for the following:

(a) a combination of (I) with an antidiabetic compound (as described above) for simultaneous, sequential or separate use;

(b) compositions comprising (I) with the antidiabetic compound; and

(c) a composition capable of being granulated in the presence of water without the need for a subsequent pulverization step prior to tabletting, comprising (I) and a carrier; and its use for treating a metabolic disorder.

ACTIVITY - Antidiabetic; anorectic; antilipemic; opthalmological; vasotropic; antiulcer; antiinflammatory; cardiant; hypotensive;

antianginal; dermatological; antiarthritic; osteopathic; gastrointestinal.

MECHANISM OF ACTION - None given.

USE - For treating a metabolic disorder, e.g. diabetes (particularly type II diabetes mellitus) and associated conditions, also for effecting weight loss. The compositions can be used to treat e.g. hyperglycemia, hyperinsulinemia, hyperlipidemia, insulin resistance, impaired glucose metabolism, obesity, diabetic retinopathy, macular degeneration, cataracts, diabetic nephropathy, glomerulonephritis, diabetic neuropathy, erectile dysfunction, premenstrual syndrome, vascular restenosis, ulcerative colitis, coronary heart disease, hypertension, angina pectoris, myocardial infarction, stroke, skin and connective tissue disorders, foot ulcerations, metabolic acidosis, arthritis, osteoporosis, and conditions of impaired glucose tolerance.

Dwg.0/0

TECH UPTX: 20010603

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compounds: (I) is present in the B-type or H-type **crystal** modification. The antidiabetic compound is preferably a glitazone, e.g. rosiglitazone, troglitazone or pioglitazone, or metformin or its hydrochloride. Preferred Combination: The combination may further comprise insulin, or comprises at least 2 antidiabetic compounds.

Preferred Composition: A composition comprising (I) and a carrier releases 60-95 wt.% (I) within 30 minutes in water. The composition may further comprise colloidal silicon dioxide, and a disintegrant, preferably having molecular weight greater than 1000000, and particle size distribution of less than 400 microm or less than 74 microm. The composition may be in the form of a tablet, a granular composition, or contained in a capsule.

L3 ANSWER 16 OF 16 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-281809 [29] WPIDS
DNC C2001-085742
TI Combination used for treating diabetes and metabolic disorders comprises **nateglinide**, antidiabetic phenylacetic acid derivative or acarbose and carrier.
DC B05
IN BALL, M; DUNNING, B; GATLIN, M R; PONGOWSKI, M
PA (NOVS) NOVARTIS AG; (NOVS) NOVARTIS-ERFINDUNGEN VERW GES MBH
CYC 95
PI WO 2001026639 A2 20010419 (200129)* EN 28
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001011339 A 20010423 (200147)
EP 1218015 A2 20020703 (200251) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2001026639 A2 WO 2000-EP9816 20001006; AU 2001011339 A AU 2001-11339 20001006; EP 1218015 A2 EP 2000-972695 20001006, WO 2000-EP9816 20001006
FDT AU 2001011339 A Based on WO 2001026639; EP 1218015 A2 Based on WO 2001026639
PRAI US 1999-415308 19991008; US 1999-415307 19991008
AB WO 200126639 A UPAB: 20010528

NOVELTY - Combination (I) comprises **nateglinide**, an antidiabetic phenylacetic acid derivative or acarbose or their salts and optionally at least one carrier for simultaneous, separate or sequential use.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a commercial package comprising (I) together with instructions for the delay

of progression or treatment of metabolic disorders or a method of improving bodily appearance.

ACTIVITY - Antidiabetic; antilipemic; antiulcer; antiinflammatory; vasotropic; hypotensive; cardiant; antiarthritic; osteopathic; cerebroprotective; anorectic; gastrointestinal; ophthalmological; muscular; dermatological.

MECHANISM OF ACTION - None given.

USE - Used for treating diabetes, conditions associated with diabetes, especially type 2 diabetes mellitus and metabolic disorders e.g. hyperglycemia, hyperinsulinaemia, hyperlipidemia, insulin resistance, impaired glucose metabolism, obesity, diabetic retinopathy, macular degeneration, cataracts, diabetic nephropathy, glomerulosclerosis, diabetic neuropathy, erectile dysfunction, premenstrual syndrome, vascular restenosis and ulcerative colitis, coronary heart disease, hypertension, angina pectoris, myocardial infarction, stroke, skin, connective tissue disorders, foot ulcerations, metabolic acidosis, arthritis, osteoporosis and conditions of impaired glucose tolerance.

ADVANTAGE - The **nateglinide** and phenylacetic acid derivative show a synergistic effect.

Dwg.0/0

TECH UPTX: 20010528

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Combination: The combination is a combined preparation or a pharmaceutical composition. The antidiabetic phenylacetic acid is repaglinide or its salts. The combination also comprises at least one antidiabetic thiazolidinedione, sulfonyl urea derivatives, metformin or insulin or their salts or at least one further antidiabetic phenylacetic acid derivative or its salts. The **nateglinide** is present in the B-type or H-type **crystal** modification.

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